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<p>(42) International Application Number: PCT/US92/02741 (44) International Filing Date: 6 April 1992 (06.04.92) (30) Priority data: 681,880 5 April 1991 (05.04.91) US (60) Parent Application or Grant (63) Related by Continuation US 681,880 (CIP) Filed on 5 April 1991 (05.04.91) (71) Applicant (for all designated States except US): THE TRUSTEES OF COLUMBIA UNIVERSITY IN THE CITY OF NEW YORK [US/US]; Broadway and West 116th Street, New York, NY 10027 (US).</p>	<p>(72) Inventors: and (75) Inventors/Applicants (for US only): BUCK, Linda, B. [US/US]; 100 Haven Avenue, New York, NY 10032 (US). AXEL, Richard [US/US]; 445 Riverside Drive, New York, NY 10027 (US). (74) Agent: WHITE, John, P.; Cooper & Dunham, 30 Rockefeller Plaza, New York, NY 10112 (US). (81) Designated States: AT (European patent), AU, BE (European patent), CA, CH (European patent), DE (European patent), DK (European patent), ES (European patent), FR (European patent), GB (European patent), GR (European patent), IT (European patent), JP, LU (European patent), MC (European patent), NL (European patent), SE (European patent), US. Published With international search report.</p>	
<p>(54) Title: ODORANT RECEPTORS AND USES THEREOF</p> <p>(57) Abstract</p> <p>The invention provides an isolated nucleic acid, e.g. cDNA encoding an odorant receptor. The invention further provides expression vectors containing such nucleic acid. Also provided is a purified protein encoding an odorant receptor, with the aforementioned expression vectors and the resulting transformed cell. The invention also provides methods of identifying odorant ligands and of identifying odorant receptors. The invention further provides methods of developing fragrances, of identifying appetite suppressant compounds, of controlling appetite, of controlling pest populations, of promoting and inhibiting fertility, and of detecting odors.</p>		



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ODORANT RECEPTORS AND USES THEREOFBackground of the Invention

5 This application is a continuation-in-part of U.S. Serial No.681,880, filed April 5, 1991, the contents of which are hereby incorporated by reference.

10 Throughout this application, various publications are referenced by Arabic numerals within parentheses. Full citations for these publications may be found at the end of the specification immediately preceding the claims. The disclosures of these publications in their entireties are hereby incorporated by reference into this application in
15 order to more fully describe the state of the art as known to those skilled therein as of the date of the invention described and claimed herein.

20 In vertebrate sensory systems, peripheral neurons respond to environmental stimuli and transmit these signals to higher sensory centers in the brain where they are processed to allow the discrimination of complex sensory information. The delineation of the peripheral mechanisms by which environmental stimuli are transduced into neural information
25 can provide insight into the logic underlying sensory processing. Our understanding of color vision, for example, emerged only after the observation that the discrimination of hue results from the blending of information from only three classes of photoreceptors (1, 2, 3, 4). The basic
30 logic underlying olfactory sensory perception, however, has remained elusive. Mammals possess an olfactory system of enormous discriminatory power (5, 6). Humans, for example, are thought to be capable of distinguishing among thousands of distinct odors. The specificity of odor recognition is
35 emphasized by the observation that subtle alterations in the molecular structure of an odorant can lead to profound

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changes in perceived odor.

The detection of chemically distinct odorant presumably results from the association of odorous ligands with specific receptors on olfactory neurons which reside in a specialized epithelium in the nose. Since these receptors have not been identified, it has been difficult to determine how odor discrimination might be achieved. It is possible that olfaction, by analogy with color vision, involves only a few odor receptors, each capable of interaction with multiple odorant molecules. Alternatively, the sense of smell may involve a large number of distinct receptors each capable of associating with one or a small number of odorant. In either case, the brain must distinguish which receptors or which neurons have been activated to allow the discrimination between different odorant stimuli. Insight into the mechanisms underlying olfactory perception is likely to depend upon the isolation of the odorant receptors, and the characterization of their diversity, specificity, and patterns of expression.

The primary events in odor detection occur in a specialized olfactory neuroepithelium located in the posterior recesses of the nasal cavity. Three cell types dominate this epithelium (Figure 1A): the olfactory sensory neuron, the sustentacular or supporting cell, and the basal cell which is a stem cell that generates olfactory neurons throughout life (7, 8). The olfactory sensory neuron is bipolar: a dendritic process extends to the mucosal surface where it gives rise to a number of specialized cilia which provide an extensive, receptive surface for the interaction of odors with olfactory sensory neurons. The olfactory neuron also gives rise to an axon which projects to the olfactory bulb of the brain, the first relay in the olfactory system. The axons of the olfactory bulb neurons, in turn, project to

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subcortical and cortical regions where higher level processing of olfactory information allows the discrimination of odors by the brain.

5 The initial events in odor discrimination are thought to involve the association of odors with specific receptors on the cilia of olfactory neurons. Selective removal of the cilia results in the loss of olfactory response (9). Moreover, in fish, whose olfactory system senses amino acids
10 as odors, the specific binding of amino acids to isolated cilia has been demonstrated (10, 11). The cilia are also the site of olfactory signal transduction. Exposure of isolated cilia from rat olfactory epithelium to numerous odorant leads to the rapid stimulation of adenylyl cyclase
15 and elevations in cyclic AMP (an elevation in IP₃ in response to one odorant has also been observed) (12, 13, 14, 15). The activation of adenylyl cyclase is dependent on the presence of GTP and is therefore likely to be mediated by receptor-coupled GTP binding proteins (G-proteins) (16).
20 Elevations in cyclic AMP, in turn, are thought to elicit depolarization of olfactory neurons by direct activation of a cyclic nucleotide-gated, cation permeable channel (17, 18). This channel is opened upon binding of cyclic nucleotides to its cytoplasmic domain, and can therefore
25 transduce changes in intracellular levels of cyclic AMP into alterations in the membrane potential.

These observations suggest a pathway for olfactory signal transduction (Figure 1B) in which the binding of odors to
30 specific surface receptors activates specific G-proteins. The G-proteins then initiate a cascade of intracellular signalling events leading to the generation of an action potential which is propagated along the olfactory sensory axon to the brain. A number of neurotransmitter and hormone
35 receptors which transduce intracellular signals by

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activation of specific G-proteins have been identified. Gene cloning has demonstrated that each of these receptors is a member of a large superfamily of surface receptors which traverse the membrane seven times (19, 20). The
5 pathway of olfactory signal transduction (Figure 1B) predicts that the odorant receptors might also be members of this superfamily of receptor proteins. The detection of odors in the periphery is therefore likely to involve signalling mechanisms shared by other hormone or
10 neurotransmitter systems, but the vast discriminatory power of the olfactory system will require higher order neural processing to permit the perception of individual odors. This invention address the problem of olfactory perception at a molecular level. Eighteen different members of an
15 extremely large multigene family have been cloned and characterized which encodes seven transmembrane domain proteins whose expression is restricted to the olfactory epithelium. The members of this novel gene family encode the individual odorant receptors.

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SUMMARY OF THE INVENTION

The invention provides an isolated nucleic acid, e.g. a DNA and cDNA molecule, encoding an odorant receptor. The invention further provides expression vectors containing such nucleic acid. Also provided by the invention is a purified protein encoding an odorant receptor. The invention further provides a method of transforming cells which comprises transfecting a suitable host cell with a suitable expression vector containing the nucleic acid encoding the odorant receptor.

The invention also provides methods of identifying odorant ligands and of identifying odorant receptors. The invention further provides methods of developing fragrances, of identifying appetite suppressant compounds, of controlling appetite. The invention also provides methods of controlling insect and other animal populations. The invention additionally provides a method of detecting odors such as the vapors emanating from Cocaine, Marijuana, Heroin, Hashish, Angel Dust, gasoline, decayed human flesh, alcohol, gun powder explosives, plastic explosives, firearms, poisonous or harmful smoke, or natural gas.

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Description of the Figures

Figure 1. The Olfactory Neuroepithelium and a Pathway for Olfactory Signal Transduction. A. The Olfactory Neuroepithelium. The initial event in odor perception occurs in the nasal cavity in a specialized neuroepithelium which is diagrammed here. Odors are believed to interact with specific receptors on the cilia of olfactory sensory neurons. The signal generated by these initial binding events are propagated by olfactory neuron axons to the olfactory bulb. B. A Pathway of Olfactory Signal Transduction. In this scheme, the binding of an odorant molecule to an odor-specific transmembrane receptor leads to the interaction of the receptor with a GTP-binding protein ($G_{S[olf]}$). This interaction, in turn, leads to the release of the GTP-coupled α -subunit of the G-protein, which then stimulates adenylyl cyclase to produce elevated levels of cAMP. The increase in cAMP opens nucleotide-gated cation channels, thus causing an alteration in membrane potential.

Figure 2. A PCR Amplification Product Containing Multiple Species of DNA. cDNA prepared from olfactory epithelium RNA was subjected to PCR amplification with a series of different primer oligonucleotides and the DNA products of appropriate size were isolated, further amplified by PCR, and size fractionated on agarose gels (A) (For details, see text). Each of these semipurified PCR products was digested with the restriction enzyme, Hinf I, and analyzed by agarose gel electrophoresis. Lanes marked "M" contain size markers of 23.1, 9.4, 5.6, 4.4, 2.3, 2.0, 1.35, 1.08, 0.87, 0.60, 0.31, 0.28, 0.23, 0.19, 0.12 and 0.07kb. (B). Twenty-two of the 64 PCR products that were isolated and digested with Hinf I are shown here. Digestion of one of these, PCR 13, yielded a large number of fragments whose sizes summed to a value much greater than that of the undigested PCR 13

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DNA, indicating that PCR 13 might contain multiple species of DNA which are representatives of a multigene family.

Figure 3. Northern Blot Analysis with a Mixture of Twenty Probes. One μ g of polyA⁺ RNA isolated from rat olfactory epithelium, brain, or spleen was size-fractionated in formaldehyde agarose, blotted onto a nylon membrane, and hybridized with a ³²P-labeled mixture of segments of 20 cDNA clones. The DNA segments were obtained by PCR using primers homologous to transmembrane domains 2 and 7.

Figure 4. The Protein Sequences Encoded by Ten Divergent cDNA Clones. Ten divergent cDNA clones were subjected to DNA sequence analyses and the protein sequence encoded by each was determined. Amino acid residues which are conserved in 60% or more of the proteins are shaded. The presence of seven hydrophobic domains (I-VII), as well as short conserved motifs shared with other members of the superfamily, demonstrate that these proteins belong to the seven transmembrane domain protein superfamily. Motifs conserved among members of the superfamily and the family of olfactory proteins include the GN in TM1 (transmembrane domain 1), the central W of TM4, the Y near the C-terminal end of TM5, and the NP in TM7. In addition, the DRY motif C-terminal to TM3 is common to many members of the G-protein-coupled superfamily. However, all of the proteins shown here share sequence motifs not found in other members of this superfamily and are clearly members of a novel family of proteins.

Figure 5. Positions of Greatest Variability in the Olfactory Protein Family. In this diagram, the protein encoded by cDNA clone I15 is shown traversing the plasma membrane seven times with its N-terminus located extracellularly, and its C-terminus intracellularly. The

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vertical cylinders delineate the seven putative α -helices spanning the membrane. Positions at which 60% or more of the 10 clones shown in Figure 4 share the same residue as I15 are shown as white balls. More variable residues are shown as black balls. The high degree of variability encountered in transmembrane domains III, IV, and V is evident in this schematic.

Figure 6. The Presence of Subfamilies in a Divergent Multigene Family. Partial nucleotide sequences and deduced protein sequences were obtained for 18 different cDNA clones. Transmembrane domain V along with the flanking loop sequences, including the entire cytoplasmic loop between transmembrane domains V and VI, are shown here for each protein. Amino acid residues found in 60% or more of the clones in a given position are shaded (A). This region of the olfactory proteins (particularly transmembrane domain V) appears to be highly variable (see Figure 4). These proteins, however, can be grouped into subfamilies (B,C,D) in which the individual subfamily members share considerable homology in this divergent region of the protein.

Figure 7. Southern Blot Analyses with Non-crosshybridizing Fragments of Divergent cDNAs. Five μ g of rat liver DNA was digested with Eco RI (A) or Hind III (B), electrophoresed in 0.75% agarose, blotted onto a nylon membrane, and hybridized to the 32 P-labeled probes indicated. The probes used were PCR-generated fragments of: 1, clone F9 (identical to F12 in Figure 4); 2, F5; 3, F6; 4, I3; 5, I7; 6, I14; or 7, I15. The lane labeled "1-7" was hybridized to a mixture of the seven probes. The probes used showed either no crosshybridization or only trace crosshybridization with one another. The size markers on the left correspond to the four blots on the left (1-4) whereas the marker positions noted on the right correspond to the four blots on the right

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(5-7, "1-7").

- Figure 8. Northern Blot Analysis with a Mix of Seven Divergent Clones. One μ g of polyA+ RNA from each of the tissues shown was size-fractionated, blotted onto a nylon membrane, and hybridized with a 32 P-labeled mixture of segments of seven divergent cDNA clones (see Legend to Figure 7).
- Figure 9. The amino acid and nucleic acid sequence of clone F3.
- Figure 10. The amino acid and nucleic acid sequence of clone F5.
- Figure 11. The amino acid and nucleic acid sequence of clone F6.
- Figure 12. The amino acid and nucleic acid sequence of clone F12.
- Figure 13. The amino acid and nucleic acid sequence of clone I3.
- Figure 14. The amino acid and nucleic acid sequence of clone I7.
- Figure 15. The amino acid and nucleic acid sequence of clone I8.
- Figure 16. The amino acid and nucleic acid sequence of clone I9.
- Figure 17. The amino acid and nucleic acid sequence of clone I14.

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Figure 18. The amino acid and nucleic acid sequence of clone I15.

5 Figure 19. The amino acid and nucleic acid sequence of human clone H5.

10 Figure 20. The amino acid and nucleic acid sequence of clone J1, where the reading frame starts at nucleotide position 2.

Figure 21. The amino acid and nucleic acid sequence of clone J2.

15 Figure 22. The amino acid and nucleic acid sequence of clone J4, where the reading frame starts at nucleotide position 2.

20 Figure 23. The amino acid and nucleic acid sequence of clone J7, where the reading frame starts at nucleotide position 2.

25 Figure 24. The amino acid and nucleic acid sequence of clone J8, where the reading frame starts at nucleotide position 2.

Figure 25. The amino acid and nucleic acid sequence of clone J11.

30 Figure 26. The amino acid and nucleic acid sequence of clone J14, where the reading frame starts at nucleotide position 2.

35 Figure 27. The amino acid and nucleic acid sequence of clone J15, where the reading frame starts at nucleotide position 2.

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Figure 28. The amino acid and nucleic acid sequence of clone J16, where the reading frame starts at nucleotide position 2.

5 Figure 29. The amino acid and nucleic acid sequence of clone J17, where the reading frame starts at nucleotide position 2.

10 Figure 30. The amino acid and nucleic acid sequence of clone J19, where the reading frame starts at nucleotide position 2.

15 Figure 31. The amino acid and nucleic acid sequence of clone J20, where the reading frame starts at nucleotide position 2.

Figure 32. SOUTHERN BLOT: Five micrograms of DNA isolated from 1. Human placenta, 2. NCI-H-1011 neuroblastoma cells, or 3. CHP 134 neuroblastoma cells were treated with the
20 restriction enzyme A. Eco RI, B. Hind III, C. Bam HI, or D. Pst I, and then electrophoresed on an agarose gel and blotted onto a nylon membrane. The blotted DNA was hybridized to the ³²P-labeled H3/H5 sequence. An autoradiograph of the hybridized blot is shown with the
25 sizes of co-electrophoresed size markers noted in kilobases.

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Detailed Description of the Invention

The invention provides an isolated nucleic acid, e.g. a DNA or cDNA molecule, encoding an odorant receptor. Such a
5 receptor is a receptor which binds an odorant ligand and include but not limited to pheromone receptors. An odorant ligand may include, but is not limited to, molecules which interact with the olfactory sensory neuron, molecules which interact with the olfactory cilia, pheromones, and molecules
10 which interact with structures within the vomeronasal organ.

The invention specifically provides the isolated cDNAs encoding odorant receptors the sequences of which are shown in Figures 9-31. The nucleic acid is most typically a cDNA
15 and encodes an insect, a vertebrate, a fish or a mammalian odorant receptor. The mammalian odorant receptor is preferably a human, rat, mouse or dog receptor. In an embodiment, human odorant receptor cDNA sequence and the correspondent protein is isolated (Figure 19).

20 In another embodiment, pheromone receptors are isolated and shown as clones J1, J2, J4, J7, J8, J11, J14, J15, J16, J17, J19 and J20 (Figures 20-31).

25 The invention further provides expression vectors containing cDNA which encodes odorant receptors. Such expression vectors are well known in the art and include in addition to the nucleic acid the elements necessary for replication and expression in a suitable hosts. Suitable hosts are well
30 known in the art and include without limitation bacterial hosts such as E. coli, animal hosts such as CHO cells, insect cells, yeast cells and like.

The invention also provides purified proteins encoding
35 odorant receptors. Such proteins may be prepared by

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expression of the forementioned expression vectors in suitable host cells and recovery and purification of the receptors using methods well known in the art. Examples of such proteins include those having the amino acid sequences shown in figures 9-31.

The purified protein typically encodes an insect, vertebrate, fish or mammalian odorant receptor. The mammalian odorant receptor may be a human, rat, mouse or dog.

In one embodiment the invention provides a novel purified protein which belong to a class of proteins which have 7 transmembrane regions and a third cytoplasmic loop from the N-terminus which is approximately 17 amino acid long and to nucleic acid molecules encoding such proteins.

The invention provides methods of transforming cells which comprises transfecting a suitable host cell with a suitable expression vector containing nucleic acid encoding of the odorant receptor. Techniques for carrying out such transformations on cells are well known to those skilled in the art. (41,42) Additionally, the resulting transformed cells are also provided by the invention. These transformed cells may be either olfactory cells or non-olfactory cells. One advantage of using transformed non-olfactory cells is that the desired odorant receptor will be the only odorant receptor expressed on the cell's surface.

In order to obtain cell lines that express a single receptor type, standard procedures may be used to clone individual cDNAs or genes into expression vectors and then transfect the cloned sequences into mammalian cell lines. This approach has been used with sequences encoding some other members of the seven transmembrane domain superfamily

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including the 5HT1c serotonin receptor. (43) The cited work illustrates how members of this superfamily transferred into cell lines may generate immortal cell lines that express high levels of the transfected receptor on the cell surface where it will bind ligand and that such abnormally expressed receptor molecules can transduce signals upon binding to ligand.

The invention also provides a method of identifying a desired odorant ligand which comprises contacting transformed non-olfactory cells expressing a known odorant receptor with a series of odorant ligands to determining which ligands bind to the receptors present on the non-olfactory cells.

Additionally, the invention provides a method of identifying a desired odorant receptor comprising contacting a series of transformed non-olfactory cells with a known odorant ligand and determining which odorant receptor binds with the odorant ligand.

The invention provides a method of detecting an odor which comprises: a) identifying a odorant receptor which binds the desired odorant ligand and; b) imbedding the receptor in a membrane such that when the odorant ligand binds to the receptor so identified a detectable signal is produced. In one embodiment of the invention the membrane used in this method is cellular, including a membrane of an olfactory cell or a synthetic membrane.

The ligand tested for may be the vapors emanating from Cocaine, Marijuana, Heroin, Hashish, Angel Dust, gasoline, decayed human flesh, alcohol, gun powder explosives, plastic explosives or firearms. In another embodiment the ligand tested for may be natural gas, a ph romone, toxic fumes,

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noxious fumes or dangerous fumes.

In one embodiment of the invention the detectable signal is a lightbulb lighting up, a buzzer buzzing, a bell ringing,
5 a color change, phosphorescence, or radioactivity.

The invention further provides a method of quantifying the amount of an odorant ligand present in a sample which comprises utilizing the above-mentioned method for odor
10 detection and then quantifying the amount of signal produced.

The invention further provides a method of developing fragrances which comprises identifying a desired odorant
15 receptor by the above method, then contacting non-olfactory cells, which have been transfected with an expression vector containing nucleic acid encoding the desired odorant receptor such that the receptor is expressed upon the surface of the non-olfactory cell, with a series of
20 compounds to determine which compound or compounds bind the receptor.

The invention provides to a method of identifying an "odorant fingerprint" which comprises contacting a series of
25 cells, which have been transformed such that each express a known odorant receptor, with a desired sample and determining the type and quantity of the odorant ligands present in the sample.

30 The invention provides a method of identifying odorant ligands which inhibit the activity of a desired odorant receptor which comprises contacting the desired odorant receptor with a series of compounds and determining which compounds inhibit the odorant ligand - odorant receptor
35 interaction.

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The invention also provides for a method of identifying appetite suppressant compounds which comprises identifying odorant ligands by the method mentioned in the preceding paragraph wherein the desired odorant receptor is that which is associated with the perception of food. Additionally, the invention provides a method of controlling appetite in a subject which comprises contacting the olfactory epithelium of the subject with these odorant ligands. Further the invention provides a nasal spray, to control appetite comprising the compounds identified by the above method in a suitable carrier.

The invention provides a method of trapping odors which comprises contacting a membrane which contains multiples of the desired odorant receptor, with a sample such that the desired odorant ligand is absorbed by the binding of the odorant ligand to the odorant receptor. The invention also provides an odor trap employing this method.

The invention also provides a method of controlling pest populations which comprises identifying odorant ligands by the method mentioned above which are alarm odorant ligands and spraying the desired area with the identified odorant ligands. Additionally, provided by the invention is a method of controlling a pest population which comprises identifying odorant ligands by the above mentioned method, which interfere with the interaction between the odorant ligands and the odorant receptors which are associated with fertility. In one embodiment the pest population is a population of insects or rodents, including mice and rats.

The invention also provides a method of promoting fertility which comprises identifying odorant ligands which interact with the odorant receptors associated with fertility by the above mentioned method. Further, the invention provides a

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method of inhibiting fertility which comprises employing the above mentioned method to identifying odorant ligands which inhibit the interaction between the odorant ligands and the odorant receptors associated with fertility.

5

This invention is illustrated in the Experimental Detail section which follow. These sections are set forth to aid in an understanding of the invention but are not intended to, and should not be construed to, limit in any way the invention as set forth in the claims which follow thereafter.

10

EXPERIMENTAL DETAILS

15

MATERIALS AND METHODS

Polymerase Chain Reaction

20 RNA was prepared from the olfactory epithelia of Sprague Dawley rats according to Chirgwin et al. (40) or using RNazol B (Cinna/Biotech) and then treated with DNase I (0.1 unit/ μ g RNA) (Promega). In order to obtain cDNA, this RNA was incubated at 0.1 μ g/ μ l with 5 μ M random hexamers (Pharmacia) 1 mM each of dATP, dCTP, dGTP, TTP, and 2 units/ μ l RNase inhibitor (Promega) in 10 mM TrisCl (pH 8.3), 50 mM KCl, 2.5 mM MgCl₂, and 0.001% gelatin for 10 min. at 22°C, and then for a further 45 min. at 37°C following the addition of 20 u./ μ l of Moloney murine leukemia virus reverse transcriptase (BRL). After heating at 95°C for 3 min., cDNA prepared from 0.2 μ g of RNA was used in each of a series of polymerase chain reactions (PCR) containing 10 mM TrisCl (pH 8.3), 50 mM KCl, 1.5 mM MgCl₂, 0.001% gelatin, 200 μ M each of dATP, dCTP, dGTP, and TTP, 2.5 u. Taq polymerase (Perkin Elmer Cetus), and 2 μ M of each PCR

35

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primer. PCR reactions were performed according to the following schedule: 96°C for 45 sec., 55°C for 4 min. (or 45°C for 2 min.), 72°C for 3 min. with 6 sec. extension per cycle for 48 cycles. The primers used for PCR were a series of degenerate oligonucleotides made according to the amino acid sequences found in transmembrane domain 2 and 7 of a variety of different members of the 7 transmembrane domain protein superfamily (19). The regions used correspond to amino acids number 60-70 and 286-295 of clone I15 (Figure 4). Each of five different 5' primers were used in PCR reactions with each of six different 3' primers. The 5' primers had the sequences:

15 C AC A C CT
A1, AATTGGATICTIGTIAATCTIGCIGTIGCIGCIGA;

C C CA A C C
A2, AATTATTTTCTIGTIAATCTIGCITTIGCIGA;

20 CCA CC A C
A3, AATTTITTTATATITCTIGCITGIGCIGA;

A T C T ACT C
25 A4, CGITTICTIATGTGTAACCTITGCTTTGCIGA;

C CT TG
A5, ACIGTITATATACICATCTIACIATIGCIGA.

The 3' primers were:

30 TTA T CAG C C A
B1, CTGICGGTTCATIAAIAACATAIATATIGGGTT;

TG GA G G A A
35 B2, GATCGTTIAGACAACAATAIATATIGGGTT;

A G G A
B3, TCIATGTTAAAIGTIGTATAIATATIGGGTT;

40 T G G A A
B4, GCCTTIGTAAAIATIGCATAIAGGAAIGGGTT;

G AGA G G G A
45 B5, AAATCIGGGCTICGICAATAIATCAIIGGGTT;
CT CT G G G G A

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B6, GAIGAICCIACAAAAAATAIATAAAIGGGTT.

5 An aliquot of each PCR reaction was analyzed by agarose gel electrophoresis and bands of interest were amplified further by performing PCR reactions on pipet tip (approx. 1 μ l) plugs of the agarose gels containing those DNAs. Aliquots of these semi-purified PCR products were digested with the restriction enzymes Hae III or Hinf I and the digestion products were compared with the undigested DNAs on agarose gels.

Isolation and Analysis of cDNA Clones

15 CDNA libraries were prepared according to standard procedures (41, 42) in the cloning vector, λ ZAP II (Stratagene) using poly A⁺ RNA prepared from Sprague Dawley rat epithelia (see above) or from an enriched population of olfactory neurons which had been obtained by a 'panning' procedure, using an antibody against the H blood group antigen (Chembiomed) found on a large percentage of rat olfactory neurons. In initial library screens, 8.5×10^5 independent clones from the olfactory neuron library and 1.8×10^6 clones from the olfactory epithelium library were screened (41) with a ³²P-labeled probe (prime-it, Stratagene) consisting of a pool of gel-isolated PCR products obtained using primers A4 and B6 (see above) in PCR reactions using as template, olfactory epithelium cDNA, rat liver DNA, or DNA prepared from the two cDNA libraries. In later library screens, a mixture of PCR products obtained from 20 cDNA clones with the A4 and B6 primers was used as probe ('P1' probe). In initial screens, phage clones were analyzed by PCR using primers A4 and B6 and those which showed the appropriate size species were purified. In later screens, all position clones were purified, but only those that could be amplified with the B6 primer and a primer

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specific for vector sequence were analyzed further. To obtain plasmids from the isolated phage clones, phagemid rescue was performed according to the instructions of the manufacturer of λ ZAP II (Stratagene). DNA sequence analysis was performed on plasmid DNAs using the Sequenase system (USB), initially with the A4 and B6 primers and later with oligonucleotide primers made according to sequences already obtained.

10 Northern and Southern Blot Analyses

For Northern blots, poly A⁺ RNAs from various tissues were prepared as described above or purchased from Clontech. One μ g of each RNA was size fractionated on formaldehyde agarose gels and blotted onto nylon membranes (41, 42). For Southern blots, genomic DNA prepared from Sprague Dawley rat liver was digested with the restriction enzymes Eco RI or Hind III, size fractionated on agarose gels and blotted onto nylon membranes (41, 42). The membranes were dried at 80°C, and then prehybridized in 0.5 M sodium phosphate buffer (pH 7.3) containing 1% bovine serum albumin and 4% sodium dodecyl sulfate. Hybridization was carried out in the same buffer at 65°-70°C for 14-20 hrs. with DNAs labeled with ³²P. For the first Northern blot shown, the 'P1' probe (see above under cDNA clone isolation) was used. For the second Northern blot shown, a mix of PCR fragments from seven divergent cDNA clones was used. For Southern blots, the region indicated in clone I15 by amino acids 118 through 251 was amplified from a series of divergent cDNA clones using PCR. The primers used for these reactions had the sequences:

P1, ATGGCITATGATCGITATGTIGC, and

35 P4, AAIAGIGAIACIATIGAIAGATGIGAICC

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These DNAs (or a DNA encompassing transmembrane domains 2 through 7 for clone F6) were labeled and tested for crosshybridization at 70°C. Those DNAs which did not show appreciable crosshybridization were hybridized individually, or as a pool to Southern blots at 70°C.

Rat Sequences used to obtain similar sequences expressed in Humans

There are genes similar to the rat genes discussed above present in humans, these genes may be readily isolated by screening human gene libraries with the cloned rat sequences or by performing PCR experiments on human genomic DNA with primers homologous to the rat sequences. First, PCR experiments were performed with genomic DNA from rat, human, mouse, and several other species. When primers homologous to transmembrane domains 2 and 6 (the A4/B6 primer set used to isolate the original rat sequences) were used, DNA of the appropriate size was amplified from rat, human and mouse DNAs. When these primary PCR reactions were subsequently diluted and subjected to PCR using primers to internal sequences (P1 and P4 primers), smaller DNA species were amplified whose size was that seen when the same primers were used in PCR reactions with the cloned rat cDNAs. Similarly, when the secondary PCR was performed with one outer primer together with one inner primer (ie. A4/P4 or P1/B6), amplified DNAs were obtained whose sizes were also consistent with the amplification of genes similar in sequence and organization to the cloned rat cDNAs. Second, a mix of segments from 20 of the rat cDNAs ('P1" probe) was used to screen libraries constructed from human genomic DNAs. Hybridization under high or low stringency conditions reveals the presence of a large number of cloned human DNA segments that are homologous to the rat sequences. Finally, RNA from a human olfactory tumor (neuroesthesioma,

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NCI-H-1011) cell line has been examined for sequences homologous to those cloned in the rat. cDNA prepared from this RNA was subjected to PCR with the A4/B6 primer set and a DNA species of the appropriate size was seen. This DNA
5 was subcloned and partially sequenced and clearly encodes a member of the olfactory protein family identified in the rat.

The inserted sequence in human clones H3/H5 was amplified by
10 PCR with the A4/B6 primers, gel purified, and then labeled with 32P. The labeled DNA was then hybridized to restriction enzyme human placenta. Multiple hybridizing species were observed with each DNA (See Figure 32). This observation is consistent with the presence of a family of
15 odorant receptor genes in the human genome.

The sequence of clone H5 is hereby shown in Figure 19. In addition, the translated protein sequence is shown in Figure
20 19.

In order to identify odorant receptors in other species, degenerated primer oligonucleotides homologous to conserved regions within the rat odorant receptor family may be used in PCR reactions with genomic DNA or with cDNA prepared from
25 olfactory tissue RNA from those species.

RESULTS

Cloning the Gene Family

30 A series of degenerate oligonucleotides were designated which could anneal to conserved regions of members of the superfamily of G-protein coupled seven transmembrane domain receptor genes. Five degenerate oligonucleotides (A1-5; see Experimental Procedures) matching sequences within
35 transmembrane domain 2, and six degenerate oligonucleotides

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(B1-6) matching transmembrane domain 7 were used in all combinations in PCR reactions to amplify homologous sequences in cDNA prepared from rat olfactory epithelium RNA. The amplification products of each PCR reaction were then analyzed by agarose gel electrophoresis. Multiple bands were observed with each of the primer combinations. The PCR products within the size range expected for this family of receptors (600 to 1300 bp) were subsequently picked and amplified further with the appropriate primer pair in order to isolate individual PCR bands. Sixty-four PCR bands isolated in this fashion revealed only one or a small number of bands upon agarose gel electrophoresis. Representatives of these isolated PCR products are shown in Figure 2A.

The isolated PCR products were digested with the endonuclease, Hae III or Hinf I, which recognize four base restriction sites and cut DNA at frequent intervals. In most instances, digestion of the PCR product with Hinf I generated a set of fragments whose molecular weights sum to the size of the original DNA (Figure 2B). These PCR bands are therefore likely to each contain a single DNA species. In some cases, however, restriction digestion yielded a series of fragments whose molecular weights sum to a value greater than that of the original PCR product. The most dramatic example is shown in Figure 2 where the 710 bp, PCR 13 DNA, is cleaved by Hinf I to yield a very large number of restriction fragments whose sizes sum to a value five- to ten-fold greater than that of the original PCR product. These observations indicated that PCR product 13 consists of a number of different species of DNA, each of which could be amplified with the same pair of primer oligonucleotides. In addition, when PCR experiments similar to those described were performed using cDNA library DNAs as templates, a 710 bp PCR product was obtained with the PCR13 primer pair

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(A4/B6) with DNA from olfactory cDNA libraries, but not a glioma cDNA library. Moreover, digestion of one of this 710 bp product also revealed the presence of multiple DNA species. In other cases (see PCR product 20, for example),
5 digestion yielded a series of restriction fragments whose molecular weights also sum to a size greater than the starting material. Further analysis, however, revealed that the original PCR product consisted of multiple bands of similar but different sizes.

10

In order to determine whether the multiple DNA species present in PCR 13 encode members of a family of seven transmembrane domain proteins, PCR 13 DNA was cloned into the plasmid vector Bluescript and five individual clones
15 were subjected to DNA sequence analysis. Each of the five clones exhibited a different DNA sequence, but each encoded a protein which displayed conserved features of the superfamily of seven transmembrane domain receptor proteins. In addition, the proteins encoded by all five clones shared
20 distinctive sequence motifs not found in other superfamily members indicating they were all members of a new family of receptors.

To obtain full-length cDNA clones, cDNA libraries prepared
25 from olfactory epithelium RNA or from RNA of an enriched population of olfactory sensory neurons were screened. The probe used in these initial screens was a mixture of PCR 13 DNA as well as DNA obtained by amplification of rat genomic DNA or DNA from two olfactory cDNA libraries with the same
30 primers used to generate PCR 13 (A4 and B6 primers). Hybridizing plaques were subjected to PCR amplification with the A4/B6 primer set and only those giving a PCR product of the appropriate size (approximately 710 bp) were purified. The frequency of such positive clones in the enriched
35 olfactory neuron cDNA library was approximately five times

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greater than the frequency in the olfactory epithelium cDNA library. The increased frequency of positive clones observed in the olfactory neuron library is comparable to the enrichment in olfactory neurons generally obtained in the purification procedure.

The original pair of primers used to amplify PCR 13 DNA were then used to amplify coding segments of 20 different cDNA clones. A mix of these PCR products were labeled and used as probe for further cDNA library screens. This mixed probe was also used in a Northern blot (Figure 3) to determine whether the expression of the gene family is restricted to the olfactory epithelium. The mixed probe detects two diffuse bands centered at 2 and 5 kb in RNA from olfactory epithelium; no hybridization can be detected in brain or spleen. (Later experiments which examined a larger number of tissue RNAs with a more restricted probe will be shown below.) Taken together, these data indicate the discovery of a novel multigene family encoding seven transmembrane domain proteins which are expressed in olfactory epithelium, and could be expressed predominantly or exclusively in olfactory neurons.

The Protein Sequences of Numerous, Olfactory-specific Members of the Seven Transmembrane Domain Superfamily

Numerous clones were obtained upon screening cDNA libraries constructed from olfactory epithelium and olfactory neuron RNA at high stringency. Partial DNA sequences were obtained from 36 clones; 18 of these cDNA clones are different, but all of them encode proteins which exhibit shared sequence motifs indicating that they are members of the family identified in PCR 13 DNA. A complete nucleotide sequence was determined for coding regions of ten of the most divergent clones (Figure 4). The deduced protein sequences

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of these cDNAs defines a new multigene family which shares sequence and structural properties with the superfamily of neurotransmitter and hormone receptors that traverse the membrane seven times. This novel family, however, exhibits
5 features different from any other member of the receptor superfamily thus far identified.

Each of the ten sequences contains seven hydrophobic stretches (19-26 amino acids) that represent potential
10 transmembrane domains. These domains constitute the regions of maximal sequence similarity to other members of the seven transmembrane domain superfamily (see legend to Figure 4). On the basis of structural homologies with rhodopsin and the β -adrenergic receptors, (19) it is likely that the amino
15 termini of the olfactory proteins are located on the extracellular side of the plasma membrane and the carboxyl termini are located in the cytoplasm. In this scheme, three extracellular loops alternate with three intracellular loops to link the seven transmembrane domains (see Figure 5).
20 Analysis of the sequences in figure 4 demonstrates that the olfactory proteins, like other members of the receptor superfamily, display no evidence of an N-terminal signal sequence. As in several other superfamily members, a potential N-linked glycosylation site is present in all ten
25 proteins within the short N-terminal extracellular segment. Other structural features conserved with previously identified members of the superfamily included cysteine residues at fixed positions within the first and second extracellular loops that are thought to form a disulfide
30 bond. Finally, many of the olfactory proteins reveal a conserved cysteine within the C-terminal domain which may serve as a palmitoylation site anchoring this domain to the membrane (21). These features, taken together with several short, conserved sequence motifs (see legend to Figure 4),
35 clearly define this new family as a member of the

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superfamily of genes encoding the seven transmembrane domain receptors.

5 There are, however, important differences between the olfactory protein family and the other seven transmembrane domain proteins described previously and these differences may be relevant to proposed function of these proteins in odor recognition. Structure-function experiments involving in vitro mutagenesis suggest that adrenergic ligands
10 interact with this class of receptor molecule by binding within the plane of the membrane (22, 20). Not surprisingly, small receptor families that bind the same class of ligands, such as the adrenergic and muscarinic acetylcholine receptor families exhibit maximum sequence
15 conservation (often over 80%) within the transmembrane domains. In contrast, the family of receptors discussed in this application shows striking divergence within the third, fourth, and fifth transmembrane domains (Figure 4). The variability in the three central transmembrane domains is
20 highlighted schematically in Figure 5. The divergence in potential ligand binding domains is consistent with the idea that the family of molecules cloned is capable of associating with a large number of odorant of diverse molecular structure.

25 Receptors which belong to the superfamily of seven transmembrane domain proteins interact with G-proteins to generate intracellular signals. In vitro mutagenesis experiments indicate that one site of association between
30 receptor and G-protein resides within the third cytoplasmic loop (22, 23). The sequence of this cytoplasmic loop in 18 different clones we have characterized is shown in Figure 6A. This loop which is often quite long and of variable length in the receptor superfamily is relatively short (only
35 17 amino acids) and of fixed length in the 18 clones

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examined. Eleven of the 18 different clones exhibit the sequence motif K/R I V S S I (or a close relative) at the N-terminus of this loop. Two of the cDNA clones reveal a different H I T C/W A V motif at this site. If this short
5 loop is a site of contact with G-proteins, it is possible that the conserved motifs may reflect sites of interaction with different G-proteins that activate different intracellular signalling systems in response to odors. In addition, the receptors cloned reveal several serine or
10 threonine residues within the third cytoplasmic loop. By analogy with other G-protein coupled receptors, these residues may represent sites of phosphorylation for specific receptor kinases involved in desensitization. (24)

15 Subfamilies within the Multigene Family

Figure 6A displays the sequences of the fifth transmembrane domain and the adjacent cytoplasmic loop encoded by L8 of the cDNA clones we have analyzed. As a group, the 18
20 sequences exhibit considerable divergence within this region. The multigene family, however, can be divided into subfamilies such that the members of a given subfamily share significant sequence conservation. In subfamily B, clones F12 and F13, for example, differ from one another at only
25 four of 44 positions (91% identify), and clearly define a subfamily. Clones F5 and I11 (subfamily D) differ from F12 and F13 at 34-36 positions within this region and clearly define a separate subfamily. Thus, this olfactory-specific multigene family consists of highly divergent subfamilies.
30 If these genes encode odor receptors, it is possible that members of the divergent subfamilies bind odorant of widely differing structural classes. Members of the individual subfamilies could therefore recognize more subtle differences between molecules which belong to the same
35 structural class of molecules structures.

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The Size of the Multigene Family

Genomic Southern blotting experiments were performed and genomic libraries were screened to obtain an estimate of the sizes of the multigene family and the member subfamilies encoding the putative odor receptors. DNAs extending from the 3' end of transmembrane domain 3 to the middle of transmembrane domain 6 were synthesized by PCR from DNA of seven of the divergent cDNA clones (Figure 4). In initial experiments, these DNAs were labeled and hybridized to each other to define conditions under which minimal crosshybridization would be observed among the individual clones. At 70°C, the seven DNAs showed no crosshybridization, or crosshybridized only very slightly. The trace levels of crosshybridization observed are not likely to be apparent upon genomic Southern blot analysis where the amounts of DNA are far lower than in the test cross.

Probes derived from these seven DNAs were annealed under stringent conditions, either individually or as a group, to Southern blots of rat liver DNA digested with the restriction endonucleases Eco RI or Hind III (Figure 7). Examination of the Southern blots reveals that all but one of the cDNAs detects a relatively large, distinctive array of bands in genomic DNA. Clone I15 (probe 7), for example, detects about 17 bands with each restriction endonuclease, whereas clone F9 (probe 1) detects only about 5-7 bands with each enzyme. A single band is obtained with clone I7 (probe 5). PCR experiments using nested primers (TM2/TM7 primers followed by primers to internal sequences) and genomic DNA as template indicate that the coding regions of the members of this multigene family, like those of many members of the G-protein coupled superfamily, may not be interrupted by introns. This observation, together with the fact that most

-30-

of the probes only encompasses 400 nucleotides suggests that each band observed in these experiments is likely to represent a different gene. These data suggest that the individual probes chosen are representatives of subfamilies which range in size from a single member to as many as 17 members. A total of about 70 individual bands were detected in this analysis which could represent the presence of at least 70 different genes. Although the DNA probes used in these blots did not crosshybridize appreciably with each other, it is possible that a given gene might hybridize to more than one probe, resulting in an overestimate of gene number. However, it is probable that the total number of bands only reflects a minimal estimate of gene number since it is unlikely that we have isolated representative cDNAs from all of the potential subfamilies and the hybridizations were performed under conditions of very high stringency.

A more accurate estimate of the size of the olfactory-specific gene family was obtained by screening rat genomic libraries. The mix of the seven divergent probes used in Southern blots, or the mix of 20 different probes used in our initial Northern blots (see Figure 3), were used as hybridization probes under high (65°C) or lowered (55°C) stringency conditions in these experiments. Nested PCR (see above) was used to verify that the clones giving a positive signal under low stringency annealing conditions were indeed members of this gene family. It is estimated from these studies that there are between 100 and 200 positive clones per haploid genome. The estimate of the size of the family obtain from screens of genomic libraries again represents a lower limit. Given the size of the multigene family, one might anticipate that many of these genes are linked such that a given genomic clone may contain multiple genes. Thus the data from Southern blotting and screens of genomic libraries indicate that the multigene family identified

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consists of one to several hundred member genes which can be divided into multiple subfamilies.

It should be noted that the cDNA probes isolated may not be representative of the full complement of subfamilies within the larger family of olfactory proteins. The isolation of cDNAs, for example, relies heavily on PCR with primers from transmembrane domains 2 and 7 and biases our clones for homology within these regions. Thus, estimates of gene number as well as subsequent estimates of RNA abundance should be considered as minimal.

Expression of the Members of this Multigene Family

Additional Northern blot analyses were performed to demonstrate that expression of the members of this gene family is restricted to the olfactory epithelium. (Figure 8) Northern blot analysis with a mixed probe consisting of the seven divergent cDNAs used above reveals two diffuse bands about 5 and 2 kb in length in olfactory epithelium RNA. This pattern is the same as that seen previously with the mix of 20 DNAs. No annealing is observed to RNA from the brain or retina or other, nonneural tissues, including lung, liver, spleen, and kidney.

An estimate of the level of expression of this family can be obtained from screens of cDNA libraries. The frequency of positive clones in cDNA libraries made from olfactory epithelium RNA suggests that the abundance of the RNAs in the epithelium is about one in 20,000. The frequency of positive clones is approximately five-fold higher in a cDNA library prepared from RNA from purified olfactory neurons (in which 75% of the cells are olfactory neurons). The increased frequency of positive clones obtained in the olfactory neuron cDNA library is comparable to the

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enrichment we obtain upon purification of olfactory neurons. These observations suggest that this multigene family is expressed largely, if not solely, in olfactory neurons and may not be expressed in other cell types within the epithelium. If each olfactory neuron contains 10^5 mRNA molecules, from the frequency of positive clones we predict that each neuron contains only 25-30 transcripts derived from this gene family. Since the family of olfactory proteins consists of a minimum of a hundred genes, a given olfactory neuron could maximally express only a proportion of the many different family members. These values thus suggest that olfactory neurons will exhibit significant diversity at the level of expression of these olfactory proteins.

Identification of pheromone receptors in vomeronasal organ
The vomeronasal organ (vomeronasal gland) is an accessory olfactory structure that is located near the nasal cavity. Like the olfactory epithelium of the nasal cavity, the olfactory epithelium of the vomeronasal organ contains olfactory sensory neurons. The vomeronasal organ is believed to play an important role in the sensing of pheromones in numerous species. Pheromones are believed to have profound effects on both physiological and behavioral aspects of reproduction. the identification of pheromone receptors would permit the identification of the pheromones themselves. It would also enable one to identify agonists or antagonists that would either mimic the pheromones or block the pheromone receptors from transducing pheromone signals. Such information would be important to the development of species specific pesticides and, conversely, to animal husbandry. The identification of pheromone receptors in human could ultimately lead to the development of contraceptives or to treatments for infertility in humans. It is likely that the identification of pheromone receptors

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in low mammals such as rodents would lead to the identification of similar receptors in human.

5 In order to identify potential pheromone receptors, we isolate RNA from the vomeronasal organs of female rats and prepared cDNA from this RNA. The cDNA was subjected to PCR with several different pairs of degenerate oligonucleotide primers that match sequences present in the rat odorant receptor family. The PCR products were subcloned and the
10 nucleotide sequences of the subcloned DNAs were determined. Each of the subcloned DNAs encodes a protein that belongs to the odorant receptor family. The sequences of the following vomeronasal subclones are shown: J1, J2, J4, J7, J8, J11, J14, J15, J16, J17, J19, J20. In a few cases (J2, J4), the
15 same sequence was amplified with two different primer pairs and the sequence shown is a composite of the two sequences. It is possible that one or more of these molecules, or closely related molecules, serve as pheromone receptors in the rat.

20

DISCUSSION

The mammalian olfactory system can recognize and discriminate a large number of odorous molecules.
25 Perception in this system, as in other sensory systems, initially involves the recognition of external stimuli by primary sensory neurons. This sensory information is then transmitted to the brain where it is decoded to permit the discrimination of different odors. Elucidation of the logic
30 underlying olfactory perception is likely to require the identification of the specific odorant receptors, the analysis of the extent of receptor diversity and receptor specificity, as well as an understanding of the pattern of receptor expression in the olfactory epithelium.

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The odorant receptors are thought to transduce intracellular signals by interacting with G-proteins which activate second messenger systems (12, 13, 14, 15). These proteins are clearly members of the family of G-protein coupled receptors which traverse the membrane seven times (19). The odorant receptors should be expressed specifically in the tissue in which odorant are recognized. The family of olfactory proteins cloned is expressed in the olfactory epithelium. Hybridizing RNA is not detected in brain or retina, or in a host of nonneural tissues. Moreover, expression of this gene family the epithelium may be restricted to olfactory neurons. The family of odorant receptors must be capable of interacting with extremely diverse molecular structures. The genes cloned are members of any extremely large multigene family which exhibit variability in regions thought to be important in ligand binding. The possibility that each member of this large family of seven transmembrane proteins is capable of interacting with only one or a small number of odorant provides a plausible mechanism to accommodate the diversity of odor perception. The properties of the gene family identified suggests that this family is likely to encode a large number of distinct odorant receptors.

25 Size of the Multigene Family

The size of the receptor repertoire is likely to reflect the range of detectable odors and the degree of structural specificity exhibited by the individual receptors. It has been estimated that humans can identify over 10,000 structurally-distinct odorous ligands. However, this does not necessarily imply that humans possess an equally large repertoire of odorant receptors. For example, binding studies in lower vertebrates suggest that structurally-related odorant may activate the same receptor molecules.

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In fish which smell amino acids, the binding of alanine to isolated cilia can be competed by other small polar residues (threonine and serine), but not by the basic amino acids, lysine or arginine (11). These data suggest that individual
5 receptors are capable of associating with several structurally-related ligands, albeit with different affinities. Stereochemical models of olfactory recognition in mammals (25) (based largely on psychophysical, rather than biophysical data) have suggested existence of several
10 primary odor groups including camphoraceous, musky, peppermint, ethereal, pungent, and putrid. In such a model, each group would contain odorant with common molecular configurations which bind to common receptors and share similar odor qualities.

15 Screens of genomic libraries with mixed probes consisting of divergent family members detect approximately 100 to 200 positive clones per genome. The present estimate of at least 100 genes provides only a lower limit since it is
20 likely that the probes used do not detect all of the possible subfamilies. Moreover, it is probable that many of these genes are linked such that a given genomic clone may contain multiple genes. It is therefore expected that the actual size of the gene family may be considerably higher
25 and this family of putative odorant receptors could constitute one of the largest gene families in the genome.

The characterization of a large multigene family encoding putative odorant receptors suggests that the olfactory
30 system utilizes a far greater number of receptors than the visual system. Color vision, for example, allows the discrimination of several hundred hues, but is accomplished by only three different photoreceptors (1, 2, 3 and 4). The photoreceptors each have different, but overlapping
35 absorption spectra which cover the entire spectrum of

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visible wavelengths. Discrimination of color results from comparative processing of the information from these three classes of photoreceptors in the brain. Whereas three photoreceptors can absorb light across the entire visible spectrum, our data suggest that a small number of odorant receptors cannot recognize and discriminate the full spectrum of distinct molecular structures perceived by the mammalian olfactory system. Rather, olfactory perception probably employs an extremely large number of receptors each capable of recognizing a small number of odorous ligands.

Diversity within the Gene Family and the Specificity of Odor Recognition

The olfactory proteins identified in this application are clearly members of the superfamily of receptors which traverse the membrane seven time. Analysis of the proteins encoded by the 18 distinct cDNAs we have cloned reveals structural features which may render this family particularly well suited for the detection of a diverse array of structurally distinct odorant. Experiments with other members of this class of receptors suggest that the ligand binds to its receptor within the plane of the membrane such that the ligand contacts many, if not all of the transmembrane helices. The family of olfactory proteins can be divided into several different subfamilies which exhibit significant sequence divergence within the transmembrane domains. Nonconservative changes are commonly observed within blocks of residues in transmembrane regions 3, 4, and 5 (Figures 4, 5, 6); these blocks could reflect the sites of direct contact with odorous ligands. Some members, for example, have acidic residues in transmembrane domain 3, which in other families are thought to be essential for binding aminergic ligands (20) while other members maintain hydrophobic residues at these positions.

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This divergence within transmembrane domains may reflect the fact that the members of the family of odorant receptors must associate with odorant of widely different molecular structures.

5

These observations suggest a model in which each of the individual subfamilies encode receptors which bind distinct structural classes of odorant. Within a given subfamily, however, the sequence differences are far less dramatic and are often restricted to a small number of residues. Thus, the members of a subfamily may recognize more subtle variations among odor molecules of a given structural class. At a practical level, individual subfamilies may recognize grossly different structures such that one subfamily may associate, for example, with the aromatic compound, benzene and its derivatives, whereas a second subfamily may recognize odorous, short chain, aliphatic molecules. Subtle variations in the structure of the receptors within, for example, the hypothetical benzene subfamily could facilitate the recognition and discrimination of various substituted derivatives such as toluene, xylene or phenol. It should be noted that such a model, unlike previous stereochemical models, does not necessarily predict that molecules with similar structures will have similar odors. The activation of distinct receptors with similar structures could elicit different odors, since perceived odor will depend upon higher order processing of primary sensory information.

Evolution of the Gene Family and the Generation of Diversity

30

Preliminary evidence from PCR analyses suggests that members of this family of olfactory proteins are conserved in lower vertebrates as well as invertebrates. This gene family presumably expanded over evolutionary time providing mammals with the ability to recognize an increasing diversity of

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odorant. Examination of the sequences of the family members cloned from mammals provides some insight into the evolution of this multigene family. Although the chromosomal loci encoding these genes has yet to be characterized, it is likely that at least some member genes will be tandemly arranged in a large cluster as is observed with other large multigene families. A tandem array of this sort provides a template for recombination events including unequal crossing over and gene conversion, that can lead to expansion and further diversification of the sort apparent among the family members we have cloned (26).

The multigene family encoding the olfactory proteins is large: all of the member genes clearly have a common ancestral origin, but have undergone considerable divergence such that individual genes encode proteins that share from 40-80% amino acid identity. Subfamilies are apparent with groups of genes sharing greater homology among themselves than with members of other subfamilies. Examination of the sequences of even the most divergent subfamilies, however, reveals a pattern in which several blocks of conserved residues are interspersed with variable regions. This segmental homology is conceptually similar to the organization of framework and hypervariable domains within the families of immunoglobulin and T cell receptor variable region sequences (27, 28). This analogy goes beyond structural organization and may extend to the function of these two gene families: each family consists of a large number of genes which have diversified over evolutionary time to accommodate the binding of a highly diverse array of ligands. The evolutionary mechanisms responsible for the diversification and maintenance of these large gene families may also be similar. It has been suggested that gene conversion has played a major role in the evolution of immunoglobulin and T cell receptor variable domains (29, 30

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- and 31). Analysis of the sequence of the putative olfactory receptors reveals at least one instance where a motif from a variable region of one subfamily is found imbedded in the otherwise divergent sequence of a second subfamily, suggesting that conversion has occurred. Such a mixing of motifs from one subfamily to another over evolutionary time would provide additional combinatorial possibilities leading to the generation of diversity.
- It should be noted, however, that the combinatorial joining of gene segments by DNA rearrangement during development, which is characteristic of immunoglobulin loci (27), is not a feature of the putative odor receptor gene family. No evidence for DNA rearrangement to generate the diversity of genes cloned has been observed. The entire coding region has been sequenced along with parts of the 5' and 3' untranslated regions of 10 different cDNA clones. The sequences of the coding regions are all different; no evidence has been obtained for constant regions that would suggest DNA rearrangement of the sort seen in the immune system. The observations indicate that the diversity olfactory proteins are coded by a large number of distinct gene sequences.
- Although it is unlikely from the data that DNA rearrangement is responsible for the generation of diversity among the putative odorant receptors, it remains possible that DNA rearrangements may be involved in the regulation of expression of this gene family. If each olfactory neuron expresses only one or a small number of genes, then a transcriptional control mechanism must be operative to choose which of the more than one hundred genes within the family will be expressed in a given neuron. Gene conversion from one of multiple silent loci into a single active locus, as observed for the trypanosome-variable surface

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glycoproteins (32), provides one attractive model. The gene conversion event could be stochastic, such that a given neuron could randomly express any one of several hundred receptor genes, or regulated (perhaps by positional information), such that a given neuron could only express one or a small number of predetermined receptor types. Alternatively, it is possible that positional information in the olfactory epithelium controls the expression of the family of olfactory receptors by more classical mechanisms that do not involve DNA rearrangement. What ever mechanisms will regulate the expression of receptor genes within this large, multigene family, these mechanisms must accommodate the requirement that olfactory neurons are regenerated every 30-60 days (8) and therefore the expression of the entire repertoire of receptors must be accomplished many times during the life of an organism.

Receptor Diversity and the Central Processing of Olfactory Information

The results suggest the existence of a large family of distinct odorant receptors. Individual members of this receptor family are likely to be expressed by only a small set of the total number of olfactory neurons. The primary sensory neurons within the olfactory epithelium will therefore exhibit significant diversity at the level of receptor expression. The question then emerges as to whether neurons expressing the same receptors are localized in the olfactory epithelium. Does the olfactory system employ a topographic map to discriminate among the numerous odorant? The spatial organization of distinct classes of olfactory sensory neurons, as defined by receptor expression, can now be determined by using the procedures of in situ hybridization and immunohistochemistry with probes specific for the individual receptor subtypes. This

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information should help to distinguish between different models that have been proposed to explain the coding of diverse odorant stimuli (33).

5 In one model, sensory neurons that express a given receptor and respond to a given odorant may be localized within defined positions within the olfactory epithelium. This topographic arrangement would also be reflected in the projection of olfactory sensory axons into discrete regions
10 (glomeruli) within the olfactory bulb. In this scheme, the central coding to permit the discrimination of discrete odorant would depend, in part, on the spatial segregation of different receptor populations. Attempts to discern the topographic localization of specific receptors at the level
15 of the olfactory epithelium has led to conflicting results. In some studies, electrophysiological recordings have revealed differences in olfactory responses to distinct odorant in different regions of the olfactory epithelium (34, 35). However, these experiments have been difficult to
20 interpret since the differences in response across the epithelium are often small and are not observed in all studies (36).

A second model argues that sensory neurons expressing
25 distinct odorant receptors are randomly distributed in the epithelium but that neurons responsive to a given odorant project to restricted regions within the olfactory bulb. In this instance, the discrimination of odors would be a consequence of the position of second order neurons in the
30 olfactory bulb, but would be independent of the site of origin of the afferent signals within the epithelium. Mapping of the topographic projections of olfactory neurons has been performed by extracellular recordings from different regions of the bulb (37, 38) and by 2-deoxyglucose
35 autoradiography to map regional activity after exposure to

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different odorant (39). These studies suggest that spatially-localized groups of bulbar neurons preferentially respond to different odorant. The existence of specific odorant receptors, randomly distributed through the olfactory epithelium, which converge on a common target within the olfactory bulb, would raise additional questions about the recognition mechanisms used to guide these distinct axonal subsets to their central targets.

Other sensory systems also spatially segregate afferent input from primary sensory neurons. The spatial segregation of information employed, for example, by the visual and somatosensory systems, is used to define the location of the stimulus within the external environment as well as to indicate the quality of the stimulus. In contrast, olfactory processing does not extract spatial features of the odorant stimulus. Relieved of the necessity to encode information about the spatial localization of the sensory stimulus, it is possible that the olfactory system of mammals uses the spatial segregation of sensory input solely to encode the identity of the stimulus itself. The molecular identification of the genes likely to encode a large family of olfactory receptors should provide initial insights into the underlying logic of olfactory processing in the mammalian nervous system.

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SEQUENCE LISTING

(1) GENERAL INFORMATION:

- (i) APPLICANT: Columbia University in the City of N.Y.,
The Trustees of
- (ii) TITLE OF INVENTION: ODORANT RECEPTORS AND USES THEREOF
- (iii) NUMBER OF SEQUENCES: 36
- (iv) CORRESPONDENCE ADDRESS:
 - (A) ADDRESSEE: COOPER & DUNHAM
 - (B) STREET: 30 Rockefeller Plaza
 - (C) CITY: New York
 - (D) STATE: New York
 - (E) COUNTRY: U.S.A.
 - (F) ZIP: 10112
- (v) COMPUTER READABLE FORM:
 - (A) MEDIUM TYPE: Floppy disk
 - (B) COMPUTER: IBM PC compatible
 - (C) OPERATING SYSTEM: PC-DOS/MS-DOS
 - (D) SOFTWARE: PatentIn Release #1.0, Version #1.25
- (vi) PRIOR APPLICATION DATA:
 - (A) APPLICATION NUMBER: US 681,880
 - (B) FILING DATE: 05-APR-1991
- (vii) ATTORNEY/AGENT INFORMATION:
 - (A) NAME: White, John P.
 - (B) REGISTRATION NUMBER: 28,678
 - (C) REFERENCE/DOCKET NUMBER: 38586
- (ix) TELECOMMUNICATION INFORMATION:
 - (A) TELEPHONE: (212) 977-9550
 - (B) TELEFAX: (212) 664-0525
 - (C) TELEX: (212) 422523 COOP UI

(2) INFORMATION FOR SEQ ID NO:1:

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 954 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: single
 - (D) TOPOLOGY: linear
- (ii) MOLECULE TYPE: cDNA
- (iii) HYPOTHETICAL: YES
- (iv) ANTI-SENSE: NO
- (v) ORIGINAL SOURCE:
 - (A) ORGANISM: rat olfactory epithelium
 - (B) STRAIN: Sprague-Dawley rat
 - (F) TISSUE TYPE: olfactory epithelium
- (vii) IMMEDIATE SOURCE:

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(B) CLONE: F12

(x1) SEQUENCE DESCRIPTION: SEQ ID NO:1:

ATGGAATCAG GGAACAGCAC AAGAAGATT TCAAGTTTT TTCTTCTTGG ATTTACAGAA	60
AACCCACAAC TTCACTTCCT CATTTTTGCA CTATTCCTGT CCATGTACCT GGTAACAGTG	120
CTTGGGAACC TGCTTATCAT TATGGCCATC ATCACACAGT CTCATTGCA TACACCCATG	180
TACTTTTTCC TTGCTAACCT ATCCTTTGTG GACATCTGTT TCACCTCCAC CACCATCCCA	240
AAGATGTTGG TAAATATATA CACCCAGAGC AAGAGCATCA CCTATGAAGA CTGTATTAGC	300
CAGATGTGTG TCTTCTTGGT TTTGCGAGAA TTGGGCAACT TTCTCCTGGC TGTGATGGCC	360
TATGACCGAT ATGTGGCTAA CTGTCACCCA CTGTGTTACA CAGTCATTGT GAACACCGG	420
CTCTGTATCC TGCTGCTTCT GCTGTCCTGG GTTATCAGCA TTTTCCATGC CTTCATACAG	480
AGCTTAATTG TGCTACAGTT GACCTTCTGT GGAGATGTGA AAATCCCTCA CTTCTTCTGT	540
GAACCTAATC AGCTGTCCCA ACTCACCTGT TCAGACAACT TTCCAAGTCA CCTCATAATG	600
AATCTTGTA CTGTTATGTT GGCAGCCATT TCCTTCAGTG GCATCCTTTA CTCTTATTTCT	660
AAGATAGTAT CCTCCATACA TTCTATCTCC ACAGTTCAGG GGAAGTACAA GGCATTTTCT	720
ACTTGTGCCT CTCACCTTTC CATGTCTCC TTATTTTATA GTACAGGCCT CGGAGTGTA	780
GTCAGTTCTG CTGTGGTCCA AAGCTCACAT TCTGCTGCAA GTGCTTCGGT CATGTATACT	840
GTGGTCACCC CCATGCTGAA CCCCTTCATT TATAGTCTAA GGAATAAAGA TGTGAAGAGA	900
GCTCTGGAAA GACTGTTAGA AGGAACTGT AAGTGCATC ATTGGACTGG ATGA	954

(2) INFORMATION FOR SEQ ID NO:2:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 1002 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA

(iii) HYPOTHETICAL: YES

(iv) ANTI-SENSE: NO

(vi) ORIGINAL SOURCE:

- (A) ORGANISM: rat olfactory epithelium
- (B) STRAIN: Sprague-Dawley rat
- (F) TISSUE TYPE: olfactory epithelium

(vii) IMMEDIATE SOURCE:

- (B) CLONE: F3

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:2:

SUBSTITUTE SHEET

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ATGGACTCAA GCAACAGGAC AAGAGTTTCA GAATTTCTTC TTCTTGGATT TGTAGAAAAC      60
AAAGACCTAC AACCCTTAT TTATGGTCTT TTTCTCTCTA TGTACCTGGT TACTGTCATT      120
GGAAACATAT CCATTATTGT GGCTATCATT TCAGATCCCT GTCTGCACAC CCCCATGTAT      180
TTCTTCCTCT CTAACCTGTC CTTTGTGGAC ATCTGTTTCA TTTCAACCAC TGTTCCAAAG      240
ATGTTAGTGA ACATCCAGAC CAAAACAAT GTCATCACCT ATGCAGGATG CATTACCCAG      300
ATATACTTTT TCTTGCTCTT TGTAGAATTG GACAACCTCT TGCTGACTAT CATGGCCTAT      360
GACCGTTACG TAGCCATCTG TCACCCCATG CACTACACAG TTATCATGAA CTACAAGCTC      420
TGTGGATTTC TGGTTCCTGGT ATCTTGGATT GTAAGTGTTT TGCATGCCTT GTTTCAAAGC      480
TTGATGATGT TGGCGCTGCC CTTCTGCACA CATCTGGAAA TCCCACACTA CTTCTGTGAA      540
CCTAATCAGG TGATTCAACT CACCTGTTCT GATGCATTTC TTAATGATCT TGTGATATAT      600
TTTACACTTG TGCTGCTGGC TACTGTTCTT CTTGCTGGCA TCTTCTATTC TTAATTCAAG      660
ATAGTGTCTT CCATATGTGC TATATCGTCA GTTCATGGGA AGTACAAAGC ATTCTCCACC      720
TGTGCATCTC ACCTTTCAGT CGTGTCTTTA TTTTACTGCA CAGGACTAGG AGTGATACCTC      780
AGTTCTGCTG CAAACAACAG CTCACAGGCA AGTGCCACAG CCTCAGTCAT GTACACTGTA      840
GTTACCCCTA TGGTGAACCC TTTTATCTAT AGTCTTAGGA ATAAAGATGT TAAGAGTGTT      900
CTGAAAAAAA CTCTTTGTGA GGAAGTTATA AGGAGTCCAC CTTCCCTACT TCATTTCTTC      960
CTAGTGTTAT GTCATCTCCC TTGTTTTATT TTTTGTATT AA                          1002

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(2) INFORMATION FOR SEQ ID NO:3:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 942 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA

(iii) HYPOTHETICAL: YES

(iv) ANTI-SENSE: NO

(vi) ORIGINAL SOURCE:

- (A) ORGANISM: rat olfactory epithelium
- (B) STRAIN: Sprague-Dawley rat
- (F) TISSUE TYPE: olfactory epithelium

(vii) IMMEDIATE SOURCE:

- (B) CLONE: F5

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:3:

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ATGAGCAGCA CCAACCAGTC CAGTGTACCC GAGTTCCTCC TCCTGGGACT CTCCAGGCAG      60
CCCCAGCAGC AGCAGCTCCT CTTCTGCTC TTCCTCATCA TGTACCTGGC CACTGTCCTG      120

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GGAAACCTGC TCATCATCCT GGCTATTGGC ACAGACTCCC GCCTGCACAC CCCCATGTAC      180
TTCTTCCTCA GTAACCTGTC CTTTGTGGAT GTCTGCTTCT CCTCTACCAC TGTCCCTAAA      240
GTTCTGGCCA ACCATATACT TGGGAGTCAG GCCATTTTCT TCTCTGGGTG TCTCACCACG      300
CTGTATTTTC TCGCTGTGTT TGGTAACATG GACAATTTCC TGCTGGCTGT GATGTCCTAT      360
GACCGATTTG TGGCCATATG CCACCCTTTA CACTACACAA CAAAGATGAC CCGTCAGCTC      420
TGTGTCCTGC TTGTTGTGGG GTCATGGGTT GTAGCCAACA TGAATTGTCT GTTGACACATA      480
CTGCTCATGG CTCGACTCTC CTTCTGTGCA GACAACATGA TCCCCCACTT CTTCTGTGAT      540
GGAATCCCC TCCTGAACT CTCCTGCTCA GACACACATC TCAATGAGCT GATGATTCTT      600
ACAGAGGGAG CTGTGGTCAT GGTACCCCCA TTTGTCTGCA TCCTCATCTC CTACATCCAC      660
ATCACCTGTG CTGTCCTCAG AGTCTCATCC CCCAGGGGAG GATGGAAATC CTTCTCCACC      720
TGTGGCTCCC ACCTGGCTGT GGTCTGCCTC TTCTATGGCA CCGTCATCGC TGTGTATTTT      780
AACCCTCAT CTCTCACTT AGCTGGGAGG GACATGGCAG CTGCAGTGAT GTATGCAGTG      840
GTGACCCCAA TGCTGAACCC TTTCATCTAT AGCCTGAGGA ACAGCGACAT GAAAGCAGCT      900
TTAAGGAAAG TGCTGCCAT GAGATTTCCA TCTAAGCAGT AA                          942

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(2) INFORMATION FOR SEQ ID NO:4:

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 936 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: single
 - (D) TOPOLOGY: linear
- (ii) MOLECULE TYPE: cDNA
- (iii) HYPOTHETICAL: YES
- (iv) ANTI-SENSE: NO
- (vi) ORIGINAL SOURCE:
 - (A) ORGANISM: rat olfactory epithelium
 - (B) STRAIN: Sprague-Dawley rat
 - (F) TISSUE TYPE: olfactory epithelium
- (vii) IMMEDIATE SOURCE:
 - (B) CLONE: F6

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:4:

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ATGGCTTGGA GTACTGGCCA GAACCTGTCC ACACCAGGAC CATTATCTT GCTGGGCTTC      60
CCAGGGCCAA GGACCATGCG CATTGGGCTC TTCCTGCTTT TCCTGGTCAT GTATCTGCTT      120
ACGGTAGTTG GAAACCTAGC CATCATCTCC CTGGTAGGTG CCCACAGATG CCTACAGACA      180
CCCATGTACT TCTTCCTCTG CAACCTCTCC TTCCTGGAGA TCTGGTTCAC CACAGCCTGC      240
GTACCCAAGA CCCTGGCCAC ATTTGCGCCT CGGGGTGGAG TCATTTCTT GGCTGGCTGT      300

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GCCACACAGA TGTACTTTGT CTTTCTTTG GGCTGTACOG AGTACTTCCT GCTGGCTGTG   360
ATGGCTTATG ACCGCTACCT GGCCATCTGC CTGCCACTGC GCTATGGTGG CATCATGACT   420
CCTGGGCTGG CGATGCGGTT GGCCCTGGGA TCCTGGCTGT GTGGGTTTTT TCGAATCACA   480
GTTCTGCTA CCCTCATTGC CCGCCTCTCT TTCTGTGGCT CACGTGTCAT CAACCACTTC   540
TTCTGTGACA TTTCGCCCTG GATAGTGCTT TCCTGCACCG ACAOGCAGGT GGTGGAAGTG   600
GTGTCCTTTG GCATTGCCTT CTGTGTTATT CTGGGCTCGT GTGGTATCAC ACTAGTCTCC   660
TATGCTTACA TCATCACTAC CATCATCAAG ATTCCCTCTG CCCGGGGCCG GCACCGGCGC   720
TTCTCAACCT GTCATCCCA TCTCACTGTG GTGCTGATT TGTATGGCTC CACCATCTTC   780
TTGCATGTGA GGACCTCGGT AGAGAGCTCC TTGGACCTCA CCAAAGCTAT CACAGTGCTC   840
AACACCATTG TCACACCTGT GCTGAACCTT TTCATATATA CTCTGAGGAA CAAGGATGTC   900
AAGGAAGCTC TGCCGAGGAC GGTGAAGGGG AAGTGA                               936

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(2) INFORMATION FOR SEQ ID NO:5:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 939 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA

(iii) HYPOTHETICAL: YES

(iv) ANTI-SENSE: NO

(vi) ORIGINAL SOURCE:

- (A) ORGANISM: rat olfactory epithelium
- (B) STRAIN: Sprague-Dawley rat
- (F) TISSUE TYPE: olfactory epithelium

(vii) IMMEDIATE SOURCE:

- (B) CLONE: I14

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:5:

```

ATGACTGGAA ATAACCAAC TTGATCTTG GAGTTCCTCC TCCTGGGTCT GCCCATCCCA   60
TCAGAGTATC ATCTCCTGTT CTATGCCCTG TTCCTGGCCA TGTACCTCAC CATCATCCTG   120
GGAAACCTGC TAATCATTGT CCTGTTCGA CTGGACTCTC ATCTCCACAT GCCCATGTAC   180
TTGTTTCTCA GCAACTTGTC CTTCTCTGAC CTCTGCTTTT CCTCTGTCAC AATGCCCAAA   240
TTGCTTCAGA ACATGCAGAG CCAAGTACCA TCTATATCCT ATACAGGCTG CCTGACACAG   300
CTGTACTTCT TTATGGTTTT TGGAGATATG GAGAGCTTCC TTCTTGTTGT CATGGCCTAT   360
GACCGCTATG TGGCCATTG CTTTCCTTTG CGTTACACCA CCATCATGAG CACCAAGTTC   420
TGTGCTTCAC TAGTGCTACT TCTGTGGATG CTGACGATGA CCCATGCCCT GCTGCATACC   480

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CTACTCATTG CTAGATTGTC TTTTGTGAG AAGAATGTGA TTCTTCACTT TTTCTGTGAC      540
ATTTCTGCTC TTCTGAAGTT GTCCTGCTCA GACATTTATG TTAATGAGCT GATGATATAT      600
ATCTTGGGTG GACTCATCAT TATTATCCCA TTCCTATTAA TTGTTATGTC CTATGTTAGA      660
ATTTTCTTCT CCATTTTGAA GTTCCATCT ATTCAGGACA TCTACAAGGT ATTCTCAACC      720
TGTGGTTCCC ATCTGTCTGT GGTGACCTTG TTTTATGGGA CAATTTTGG TATCTACTTA      780
TGTCCATCAG GTAATAATTC TACTGTGAAG GAGATTGCCA TGGCTATGAT GTACACAGTG      840
GTGACTCCCA TGCTGAATCC CTTCATCTAC AGCCTGAGGA ACAGAGACAT GAAAAGGGCC      900
CTAATAAGAG TTATCTGCAC TAAGAAAATC TCTCTGTAA                               939

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(2) INFORMATION FOR SEQ ID NO:6:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 945 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA

(iii) HYPOTHETICAL: YES

(iv) ANTI-SENSE: NO

(vi) ORIGINAL SOURCE:

- (A) ORGANISM: rat olfactory epithelium
- (B) STRAIN: Sprague-Dawley rat
- (F) TISSUE TYPE: olfactory epithelium

(vii) IMMEDIATE SOURCE:

- (B) CLONE: I15

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:6:

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ATGACAGAAG AGAACCAAAC TGTGATCTCC CAGTTCCTTC TCCTTTTCCT GCCCATCCCC      60
TCAGAGCACC AGCACGTGTT CTACGCCCTG TTCCTGTCCA TGTACCTCAC CACTGTCCTG      120
GGGAACCTCA TCATCATCAT CCTCATTAC CTGGACTCCC ATCTCCACAC ACCCATGTAC      180
TTGTTTCTCA GCAACTTGTC CTTCTCTGAT CTCTGCTTTT CCTCTGTTAC GATGCCCCAAG      240
TTGTTGCAGA ACATGCAGAG CCAAGTTCCA TCCATCCCCT TTGCAGGCTG CCTGACACAA      300
TTATACTTTT ACCTGTATTT TGCAGACCTT GAGAGCTTCC TGCTTGTTGGC CATGGCCTAT      360
GACCGCTATG TGGCCATCTG CTTCCCCCTT CATTACATGA GCATCATGAG CCCCAGCTC      420
TGTGTGAGTC TGGTGGTGCT GTCCTGGGTG CTGACCACCT TCCATGCCAT GCTGCACACC      480
CTGCTCATGG CCAGATTGTC ATTCTGTGCG GACAATATGA TCCCCCACTT TTTCTGTGAT      540
ATATCTCCTT TATTGAAACT GTCCTGCTCT GACACGCATG TTAATGAGTT GGTGATATT      600

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-55-

GTCATGGGAG GGCTTGTTAT TGTCATTCCA TTTGTGCTCA TCATTGTATC TTATGCACGA	660
GTTGTCCGCCT CCATTCTTAA AGTCCCTTCT GTCCGAGGCA TCCACAAGAT CTTCTCCACC	720
TGCGGCTCCC ATCTGTCTGT GGTGTCACTG TTCTATGGGA CAATCATTGG TCTCTACTTA	780
TGTCCGTCAG CTAATAACTC TACTGTGAAG GAGACTGTCA TGGCCATGAT GTACACAGTG	840
GTGACCCCCA TGCTGAACCC CTTTCATCTAC AGCCTGAGGA ACAGAGACAT GAAAGAGGCA	900
CTGATAAGAG TCCTTTGTAA AAAGAAAATT ACCTTCTGTC TATGA	945

(2) INFORMATION FOR SEQ ID NO:7:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 933 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA

(iii) HYPOTHETICAL: YES

(iv) ANTI-SENSE: NO

(vi) ORIGINAL SOURCE:

- (A) ORGANISM: rat olfactory epithelium
- (B) STRAIN: Sprague-Dawley rat
- (F) TISSUE TYPE: olfactory epithelium

(vii) IMMEDIATE SOURCE:

- (B) CLONE: I3

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:7:

ATGAACAATC AAACCTTCAT CACCCAATTC CTTCTCCTGG GACTGCCCAT CCCTGAAGAA	60
CATCAGCACC TGTTCATGC CTTGTTCCCTG GTCATGTACC TCACCACCAT CTTGGGAAAC	120
TTGCTAATCA TTGTACTTGT TCAACTGGAC TCCCAGCTCC ACACACCTAT GTATTTGTTT	180
CTCAGCAATT TGTCTTTCTC TGATCTATGT TTTTCCTCTG TCACAATGCC CAAGCTGCTG	240
CAGAACATGA GGAGCCAGGA CACATCCATT CCCTATGGAG GCTGCCTGGC ACAAACATAC	300
TTCTTTATGG TTTTGGAGA TATGGAGAGT TTCCTTCTTG TGGCCATGGC CTATGACCCG	360
TATGTGGCCA TCTGCTTCCC TCTGCATTAC ACCAGCATCA TGAGCCCCAA GCTCTGTACT	420
TGTCTAGTGC TGTATTGTG GATGCTGACG ACATCCCATG CCATGATGCA CACACTGCTT	480
GCAGCAAGAT TGTCTTTTGG TGAGAACAAT GTGGTCTCA ACTTCTTCTG TGACCTATTT	540
GTTCTCCTAA AGCTGGCCTG CTCAGACACT TATATTAATG AGTTGATGAT ATTTATCATG	600
AGTACACTCC TCATTATTAT TCCATTCTTC CTCATTGTTA TGTCCTATGC AAGGATCATA	660
TCCTCTATTC TTAAGGTTCC ATCTACCCAA GGCATCTGCA AGGTCTTCTC TACCTGTGGT	720

TCCCATCTGT CTGTAGTATC ACTGTTCTAT GGGACAATTA TTGGTCTCTA CTTATGTCCA	780
GCAGGTAATA ATTCCACTGT AAAAGAGATG GTCATGGCCA TGATGTACAC TGTGGTGACC	840
CCCATGCTGA ATCCCTTCAT CTACAGCCTA AGGAATAGAG ATATGAAGAG GGCCCTAATA	900
AGAGTTATCT GTAGTATGAA AATCACTCTG TAA	933

(2) INFORMATION FOR SEQ ID NO:8:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 984 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA

(iii) HYPOTHETICAL: YES

(iv) ANTI-SENSE: NO

(vi) ORIGINAL SOURCE:

- (A) ORGANISM: rat olfactory epithelium
- (B) STRAIN: Sprague-Dawley rat
- (F) TISSUE TYPE: olfactory epithelium

(vii) IMMEDIATE SOURCE:

- (B) CLONE: I7

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:8:

ATGGAGCGAA GGAACACAG TGGGAGAGTG AGTGAATTG TGTGCTGGG TTTCCCAGCT	60
CCTGCCCCAC TGCAGTACT ACTATTTTTC CTTTCTCTTC TGGACTATGT GTTGGTGTG	120
ACTGAAAACA TGCTCATCAT TATAGCAATT AGGAACCACC CAACCCTCCA CAAACCCATG	180
TATTTTTTCT TGGCTAATAT GTCATTTCTG GAGATTGGT ATGTCACGTG TACGATTCCT	240
AAGATGCTCG CTGGCTTCAT TGGTTCCAAG GAGAACCATG GACAGCTGAT CTCCTTTGAG	300
GCATGCATGA CACAACTCTA CTTTTTCCTG GGCTTGGGTT GCACAGAGTG TGTCCTTCTT	360
GCTGTGATGG CCTATGACCG CTATGTGGCT ATCTGTGATC CACTCCACTA CCCCCTCATT	420
GTCAGTAGCC GGCTATGTGT GCAGATGGCA GCTGGATCCT GGGCTGGAGG TTTTGGTATC	480
TCCATGGTTA AAGTTTTTCCT TATTTCTCGC CTGTCTTACT GTGGCCCCAA CACCATCAAC	540
CACTTTTTCT GTGATGTGTC TCCATTGCTC AACCTGTCAT GCACTGACAT GTCCACAGCA	600
GAGCTTACAG ACTTTGTCCT GGCATTTTTT ATTCTGCTGG GACCGCTCTC TGTCACGGG	660
GCATCCTACA TGGCCATCAC AGGTGCTGTG ATGCGCATCC CCTCAGCTGC TGGCCGCCAT	720
AAAGCCTTTT CAACCTGTGC CTCCCACCTC ACTGTTGTGA TCATCTTCTA TGCAGCCAGT	780
ATTTTCATCT ATGCCAGGCC TAAGGCACTC TCAGCTTTTG ACACCAACAA GCTGGTCTCT	840
GTACTCTACG CTGTCATTGT ACCGTTGTTT AATCCCATCA TCTACTGCTT GCGCAACCAA	900

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GATGTCAAAA GAGCGCTACG TCGCAOGCTG CACCTGGCCC AGGACCAGGA GGCCAATACC 960
 AACAAAGGCA GCAAAATTGG TTAG 984

(2) INFORMATION FOR SEQ ID NO:9:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 939 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA

(iii) HYPOTHETICAL: YES

(iv) ANTI-SENSE: NO

(vi) ORIGINAL SOURCE:

- (A) ORGANISM: rat olfactory epithelium
- (B) STRAIN: Sprague-Dawley rat
- (F) TISSUE TYPE: olfactory epithelium

(vii) IMMEDIATE SOURCE:

- (B) CLONE: I8

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:9:

ATGAACAACA AAAGTGTAT CACCCATTTC CTCCTCCTGG GATTGCCCAT CCCCCCAGAG 60
 CACCAGCAAC TGTTCTTTGC CCGTTCTCTG ATCATGTACC TCACCACCTT TCTGGGAAAC 120
 CTGCTAATTG TTGTCCTTGT TCAACTGGAC TCTCATCTCC ACACACCCAT GTACTTGTTC 180
 CTCAGCAACT TGTCTTCTC TGATCTCTGC TTTTCCTCTG TTACAATGCT GAAATTGCTG 240
 CAAAATATAC AGAGCCAAGT ACCATCTATA TCCTATGCAG GATGCCTGAC ACAGATATTC 300
 TTCTTTTGTG TGTTTGGCTA CCTTGGGAAT TTCCTTCTTG TAGCCATGGC CTATGACCGC 360
 TATGTGGCCA TCTGCTTCCC TCTGCATTAT ACCAACATCA TGAGCCATAA GCTCTGTACT 420
 TGTCTCCTGC TGGTATTTTG GATAATGACA TCATCTCATG CCATGATGCA CACCCTGCTT 480
 GCAGCAAGAT TGTCTTTTTC TGAGAACAAT GTACTCCTCA ACTTTTCTG TGACCTGTTT 540
 GTTCTCCTAA AGTTGGCCTG CTCAGACACT TATGTTAATG AGTTGATGAT ACATATCATG 600
 GGCCTGATCA TCATTGTTAT TCCATTCTGT CTCATTGTTA TATCCTATGC CAAGATCATC 660
 TCCTCCATTTC TTAAGGTTCC ATCTACTCAA AGCATTCAAC AGGTCTTCTC CACTGTGGT 720
 TCTCATCTCT CTGTGGTGTC TCTGTTCTAC GGGACAATTA TTGGTCTCTA TTTATGTCCA 780
 TCAGGTGATA ATTTTAGTCT AAAGGGGTCT GCCATGGCTA TGATGTACAC AGTGGTAACT 840
 CCAATGCTGA ACCCGTTCAT CTACAGCCTA AGAAACAGAG ACATGAAGCA GGCCCTAATA 900
 AGAGTTACCT GTAGCAAGAA AATCTCTCTG CCATGGTAG 939

(2) INFORMATION FOR SEQ ID NO:10:

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- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 945 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: single
 - (D) TOPOLOGY: linear
- (ii) MOLECULE TYPE: cDNA
- (iii) HYPOTHETICAL: YES
- (iv) ANTI-SENSE: NO
- (vi) ORIGINAL SOURCE:
 - (A) ORGANISM: rat olfactory epithelium
 - (B) STRAIN: Sprague-Dawley rat
 - (F) TISSUE TYPE: olfactory epithelium
- (vii) IMMEDIATE SOURCE:
 - (B) CLONE: I9

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:10:

ATGACTAGAA GAAACCAAAC TGCCATCTCT CAGTTCCTCC TTCTGGGCCT GCCATTCCCC	60
CCAGAGTACC AACACCTGTT CTATGCCCTG TTCCTGGCCA TGTACCTCAC CACTCTCCTG	120
GGGAACCTCA TCATCATCAT CCTCATTCTA CTGGACTCCC ATCTCCACAC ACCCATGTAC	180
TTGTTTCTCA GCAATTTATC CTTGCGGAC CTCTGTTTTT CCTCTGTCAC AATGCCCAAG	240
TTGTTGCAGA ACATGCAGAG CCAAGTTCCA TCCATCCCCT ATGCAGGGTG CCTGGCACAG	300
ATATACTTCT TTCTGTTTTT TGGAGACCTT GGAAACTTCC TGCTTGTTGC CATGGCCTAT	360
GACCGCTATG TGGCCATCTG CTTCCCCCTT CATTACATGA GCATCATGAG CCCCAAGCTC	420
TGTGTGAGTC TGGTGGTGCT GTCCTGGGTG CTGACTACCT TCCATGCCAT GCTGCACACC	480
CTGCTCATGG CCAGATTGTC ATTCTGTGAG GACAGTGTGA TCCCTCACTA TTTCTGTGAT	540
ATGTCTACTC TGCTGAAAGT GGCTTGTTCT GACACCCATG ATAATGAATT AGCAATATTT	600
ATCTTAGGGG GCCCTATAGT TGTACTACCT TTCCTTCTCA TCATTGTTTC TTATGCAAGA	660
ATTGTTTCCT CCATCTTCAA GGTCCCTTCT TCTCAAAGCA TCCATAAAGC CTTCTCCACC	720
TGTGGCTCCC ACCTGTCTGT GGTGTCACTG TTCTATGGGA CAGTCATTGG TCTCTACTTA	780
TGTCCTTCAG CTAATAACTC CACTGTGAAG GAGACTGTCA TGTCTTTGAT GTACACAATG	840
GTGACACCCA TGCTGAACCC CTTCATCTAC AGCCTAAGAA ACAGAGACAT AAAAGATGCA	900
TTAGAAAAAA TAATGTGCAA AAAGCAAATT CCCTCCTTTC TATGA	945

(2) INFORMATION FOR SEQ ID NO:11:

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 645 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: single
 - (D) TOPOLOGY: linear

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(ii) MOLECULE TYPE: cDNA

(iii) HYPOTHETICAL: YES

(iv) ANTI-SENSE: NO

(vi) ORIGINAL SOURCE:

(A) ORGANISM: homosapien

(vii) IMMEDIATE SOURCE:

(B) CLONE: H5

(ix) FEATURE:

(A) NAME/KEY: CDS

(B) LOCATION: 1..645

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:11:

ATC TGT TTT GTG TCT ACC ACT GTC CCA AAG CAG CTG GTG AAC ATC CAG	48
Ile Cys Phe Val Ser Thr Thr Val Pro Lys Gln Leu Val Asn Ile Gln	
1 5 10 15	
ACA CAG AGC AGA GTC ATC ACC TAT GCA GAC TGC ATC ACC CAG ATG TGC	96
Thr Gln Ser Arg Val Ile Thr Tyr Ala Asp Cys Ile Thr Gln Met Cys	
20 25 30	
TTT TTT ATA CTC TTT GTA GTG TTG GAC AGC TTA CTC CTG ACT GTG ATG	144
Phe Phe Ile Leu Phe Val Val Leu Asp Ser Leu Leu Leu Thr Val Met	
35 40 45	
GCC TAT GAC CGG TTT GTG GCC ATC TGT CAC CCC CTG CAC TAC ACA GTC	192
Ala Tyr Asp Arg Phe Val Ala Ile Cys His Pro Leu His Tyr Thr Val	
50 55 60	
ATT ATG AGC TCC TGG CTC TGT GGA CTG CTG GTT CTG GTG TCC TGG ATC	240
Ile Met Ser Ser Trp Leu Cys Gly Leu Leu Val Leu Val Ser Trp Ile	
65 70 75 80	
GTG AGC ATC CTA TAT TCT CTG TTA CAA AGC ATA ATG GCA TTG CAG CTG	288
Val Ser Ile Leu Tyr Ser Leu Leu Gln Ser Ile Met Ala Leu Gln Leu	
85 90 95	
TCC TTC TGT ACA GAA CTG AAA ATC CCT CAA TTT TTC TGT GAA CTT AAT	336
Ser Phe Cys Thr Glu Leu Lys Ile Pro Gln Phe Phe Cys Glu Leu Asn	
100 105 110	
CAG GTC ATC CAC CTT GCC TGT TCC GAC ACT TTT ATT AAT GAC ATG ATG	384
Gln Val Ile His Leu Ala Cys Ser Asp Thr Phe Ile Asn Asp Met Met	
115 120 125	
ATG AAT TTT ACA AGT GTG CTG CTG GGT GGG GGA TGC CTC GCT GGA ATA	432
Met Asn Phe Thr Ser Val Leu Leu Gly Gly Gly Cys Leu Ala Gly Ile	
130 135 140	
TTT TAC TNN TAC TTT AAG ATA CTT TGT TGC ATA TGT TCG ATC TCA TCA	480
Phe Tyr Xaa Tyr Phe Lys Ile Leu Cys Cys Ile Cys Ser Ile Ser Ser	
145 150 155 160	
GCT CAG GGG ATG AAT AAA GCA CTT TCC ACC TGT GCA TCT CAC CTC TCA	528
Ala Gln Gly Met Asn Lys Ala Leu Ser Thr Cys Ala Ser His Leu Ser	
165 170 175	

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GTT GTC TCC TTA TTT TAT TGT ACA GGC GTA GGT GTG TAC CTT AGT TCT	576
Val Val Ser Leu Phe Tyr Cys Thr Gly Val Gly Val Tyr Leu Ser Ser	
180 185 190	
GCT GCA ACC CAT AAC TCA CTC TCA AAT GCT GCA GCC TCG GTG ATG TAC	624
Ala Ala Thr His Asn Ser Leu Ser Asn Ala Ala Ala Ser Val Met Tyr	
195 200 205	
ACT GTG GTC ACC TCC ATG CTG	645
Thr Val Val Thr Ser Met Leu	
210 215	

(2) INFORMATION FOR SEQ ID NO:12:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 215 amino acids
- (B) TYPE: amino acid
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:12:

Ile Cys Phe Val Ser Thr Thr Val Pro Lys Gln Leu Val Asn Ile Gln	
1 5 10 15	
Thr Gln Ser Arg Val Ile Thr Tyr Ala Asp Cys Ile Thr Gln Met Cys	
20 25 30	
Phe Phe Ile Leu Phe Val Val Leu Asp Ser Leu Leu Leu Thr Val Met	
35 40 45	
Ala Tyr Asp Arg Phe Val Ala Ile Cys His Pro Leu His Tyr Thr Val	
50 55 60	
Ile Met Ser Ser Trp Leu Cys Gly Leu Leu Val Leu Val Ser Trp Ile	
65 70 75 80	
Val Ser Ile Leu Tyr Ser Leu Leu Gln Ser Ile Met Ala Leu Gln Leu	
85 90 95	
Ser Phe Cys Thr Glu Leu Lys Ile Pro Gln Phe Phe Cys Glu Leu Asn	
100 105 110	
Gln Val Ile His Leu Ala Cys Ser Asp Thr Phe Ile Asn Asp Met Met	
115 120 125	
Met Asn Phe Thr Ser Val Leu Leu Gly Gly Gly Cys Leu Ala Gly Ile	
130 135 140	
Phe Tyr Xaa Tyr Phe Lys Ile Leu Cys Cys Ile Cys Ser Ile Ser Ser	
145 150 155 160	
Ala Gln Gly Met Asn Lys Ala Leu Ser Thr Cys Ala Ser His Leu Ser	
165 170 175	
Val Val Ser Leu Phe Tyr Cys Thr Gly Val Gly Val Tyr Leu Ser Ser	
180 185 190	
Ala Ala Thr His Asn Ser Leu Ser Asn Ala Ala Ala Ser Val Met Tyr	
195 200 205	

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Thr Val Val Thr Ser Met Leu
210 215

(2) INFORMATION FOR SEQ ID NO:13:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 640 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA

(iii) HYPOTHETICAL: YES

(iv) ANTI-SENSE: NO

(vi) ORIGINAL SOURCE:

- (A) ORGANISM: rat olfactory epithelium
- (B) STRAIN: Sprague-Dawley rat
- (F) TISSUE TYPE: olfactory epithelium

(vii) IMMEDIATE SOURCE:

- (B) CLONE: J1

(ix) FEATURE:

- (A) NAME/KEY: CDS
- (B) LOCATION: 2..640

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:13:

C ATC TGC TTT ACT TCT GCT AGC ATC CCA AAG ATG CTA GTG AAT ATA	46
Ile Cys Phe Thr Ser Ala Ser Ile Pro Lys Met Leu Val Asn Ile	
1 5 10 15	
CAG ACG AAG AAC AAG GTG ATC ACC TAT GAA GGC TGC ATC TCC CAA GTA	94
Gln Thr Lys Asn Lys Val Ile Thr Tyr Glu Gly Cys Ile Ser Gln Val	
20 25 30	
TAC TTT TCA TAC TCT TTG GAG TTT TGG ACA ACT TTC TTC TCG ACT GTG	142
Tyr Phe Ser Tyr Ser Leu Glu Phe Trp Thr Thr Phe Phe Ser Thr Val	
35 40 45	
ATG GCC TAT GAC CGA TAT GTG GCC ATC TGT CAC CCA TCT NAC TAC ACA	190
Met Ala Tyr Asp Arg Tyr Val Ala Ile Cys His Pro Ser Xaa Tyr Thr	
50 55 60	
GGT CAT CAT GAA CCN NNN NNN NNN NNN NNN NNN NNN NNN NNN NNN NNN	238
Gly His His Glu Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa	
65 70 75	
NNN NNN NNN NNN NNN NNN NNN NNN NNN NNN NNN NNN NNN NNN NNN	286
Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa	
80 85 90 95	
NNN NNN NNN NNN NNN NNN NNN NNN NNN NNN NNN NNN NNN NNN NNN	334
Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa	
100 105 110	
NNN NNN NNN NNN NNN NNN NNN NNN NNN NNN NNN NNN NNN NNN NNN	382
Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa	

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115	120	125	
NNN NNN NNN NNN NNN NNN NNN NNN NNN NNN NNN NNN NNN NNN NTT			430
Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa			
130	135	140	
TAT TCT TAC TCT AAG ATA GTT TCC TCC ATA CGA GAA ATC TCA TCA TCA			478
Tyr Ser Tyr Ser Lys Ile Val Ser Ser Ile Arg Glu Ile Ser Ser Ser			
145	150	155	
CAG GGA AAG TAC AAG NNA TTC TCC ACC TGT GCA TCC CAC CTC TCA GTT			526
Gln Gly Lys Tyr Lys Xaa Phe Ser Thr Cys Ala Ser His Leu Ser Val			
160	165	170	175
GTT TCA TTA TTC TAT TCT ACA CTT TTG GGT GTG TAC CTT AGT TCT TCT			574
Val Ser Leu Phe Tyr Ser Thr Leu Leu Gly Val Tyr Leu Ser Ser Ser			
180	185	190	
TTT ACC CAA AAC TCA CAC TCA ACT GCA CGG GCA TCT GTT ATG TAC AGT			622
Phe Thr Gln Asn Ser His Ser Thr Ala Arg Ala Ser Val Met Tyr Ser			
195	200	205	
GTG GTC ACC CCC ATG TTG			640
Val Val Thr Pro Met Leu			
210			

(2) INFORMATION FOR SEQ ID NO:14:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 213 amino acids
- (B) TYPE: amino acid
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:14:

Ile Cys Phe Thr Ser Ala Ser Ile Pro Lys Met Leu Val Asn Ile Gln			
1	5	10	15
Thr Lys Asn Lys Val Ile Thr Tyr Glu Gly Cys Ile Ser Gln Val Tyr			
20	25	30	
Phe Ser Tyr Ser Leu Glu Phe Trp Thr Thr Phe Phe Ser Thr Val Met			
35	40	45	
Ala Tyr Asp Arg Tyr Val Ala Ile Cys His Pro Ser Xaa Tyr Thr Gly			
50	55	60	
His His Glu Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa			
65	70	75	80
Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa			
85	90	95	
Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa			
100	105	110	
Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa			
115	120	125	

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Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Tyr
 130 135 140
 Ser Tyr Ser Lys Ile Val Ser Ser Ile Arg Glu Ile Ser Ser Ser Gln
 145 150 155 160
 Gly Lys Tyr Lys Xaa Phe Ser Thr Cys Ala Ser His Leu Ser Val Val
 165 170 175
 Ser Leu Phe Tyr Ser Thr Leu Leu Gly Val Tyr Leu Ser Ser Ser Phe
 180 185 190
 Thr Gln Asn Ser His Ser Thr Ala Arg Ala Ser Val Met Tyr Ser Val
 195 200 205
 Val Thr Pro Met Leu
 210

(2) INFORMATION FOR SEQ ID NO:15:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 636 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

(iii) HYPOTHETICAL: YES

(iv) ANTI-SENSE: NO

(vi) ORIGINAL SOURCE:

- (A) ORGANISM: rat olfactory epithelium
- (B) STRAIN: srpague-Dawley rat
- (F) TISSUE TYPE: olfactory epithelium

(vii) IMMEDIATE SOURCE:

- (B) CLONE: J2

(ix) FEATURE:

- (A) NAME/KEY: CDS
- (B) LOCATION: 1..636

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:15:

ACC TCC ACC ACC ATC CCA AAG ATG CTG GTA AAT ATA CAC ACC CAG AGC	48
Thr Ser Thr Thr Ile Pro Lys Met Leu Val Asn Ile His Thr Gln Ser	
1 5 10 15	
AAT ACT ATC ACC TAT GAA GAC TGT ATT TCC CAG ATG TTT GTA CTC TTG	96
Asn Thr Ile Thr Tyr Glu Asp Cys Ile Ser Gln Met Phe Val Leu Leu	
20 25 30	
GTT TTT GGA GAA CTG GAC AAC TTT CTC CTG GCT GTG ATG GCC TAT GAT	144
Val Phe Gly Glu Leu Asp Asn Phe Leu Leu Ala Val Met Ala Tyr Asp	
35 40 45	
CGA TAT GTG GCT ATC TGT CAC CCA CTG TAT TAC ACA GTC ATT GTG AAC	192
Arg Tyr Val Ala Ile Cys His Pro Leu Tyr Tyr Thr Val Ile Val Asn	
50 55 60	

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CAC CGA CTC TGT ATC CTG CTG CTT CTG CTG TCC TGG GTT GTC AGC ATT	240
His Arg Leu Cys Ile Leu Leu Leu Leu Ser Trp Val Val Ser Ile	
65 70 75 80	
TTA CAT GCC TTC TTA CAG AGC TTA ATT GTA CTA CAG TTG ACC TTC TGT	288
Leu His Ala Phe Leu Gln Ser Leu Ile Val Leu Gln Leu Thr Phe Cys	
85 90 95	
GGA GAT GTG AAA ATC CCT CAC TTC TTC TGT GAG CTC AAT CAG CTG TCC	336
Gly Asp Val Lys Ile Pro His Phe Phe Cys Glu Leu Asn Gln Leu Ser	
100 105 110	
CAA CTC ACA TGT TCA GAC AAC TTT CCA AGT CAC CTC ACA ATG CAT CTT	384
Gln Leu Thr Cys Ser Asp Asn Phe Pro Ser His Leu Thr Met His Leu	
115 120 125	
GTA CCT GTT ATA TTT GCA GCT ATT TCC CTC AGT GGT ATC CTT TAC TCT	432
Val Pro Val Ile Phe Ala Ala Ile Ser Leu Ser Gly Ile Leu Tyr Ser	
130 135 140	
TAT TTC AAG ATA GTG TCT TCC ATA CGT TCT ATG TCC TCA GTT CAA GGG	480
Tyr Phe Lys Ile Val Ser Ser Ile Arg Ser Met Ser Ser Val Gln Gly	
145 150 155 160	
AAG TAC AAG GCA TTT TCT ACA TGT GCC TCT CAC CTT TCC ATT GTC TCC	528
Lys Tyr Lys Ala Phe Ser Thr Cys Ala Ser His Leu Ser Ile Val Ser	
165 170 175	
TTA TTT TAT AGT ACA GGC CTC GGG GTG TAC GTC AGT TCT GCT GTG ATC	576
Leu Phe Tyr Ser Thr Gly Leu Gly Val Tyr Val Ser Ser Ala Val Ile	
180 185 190	
CGA AGC TCA CAC TCC TCT GCA AGT GCT TCG GTC ATG TAT ACT GTG GTC	624
Arg Ser Ser His Ser Ser Ala Ser Ala Ser Val Met Tyr Thr Val Val	
195 200 205	
ACC CCC ATG TTG	636
Thr Pro Met Leu	
210	

(2) INFORMATION FOR SEQ ID NO:16:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 212 amino acids
- (B) TYPE: amino acid
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:16:

Thr Ser Thr Thr Ile Pro Lys Met Leu Val Asn Ile His Thr Gln Ser	
1 5 10 15	
Asn Thr Ile Thr Tyr Glu Asp Cys Ile Ser Gln Met Phe Val Leu Leu	
20 25 30	
Val Phe Gly Glu Leu Asp Asn Phe Leu Leu Ala Val Met Ala Tyr Asp	
35 40 45	
Arg Tyr Val Ala Ile Cys His Pro Leu Tyr Tyr Thr Val Ile Val Asn	

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      50              55              60
His Arg Leu Cys Ile Leu Leu Leu Leu Ser Trp Val Val Ser Ile
 65              70              75              80
Leu His Ala Phe Leu Gln Ser Leu Ile Val Leu Gln Leu Thr Phe Cys
      85              90              95
Gly Asp Val Lys Ile Pro His Phe Phe Cys Glu Leu Asn Gln Leu Ser
      100             105             110
Gln Leu Thr Cys Ser Asp Asn Phe Pro Ser His Leu Thr Met His Leu
      115             120             125
Val Pro Val Ile Phe Ala Ala Ile Ser Leu Ser Gly Ile Leu Tyr Ser
      130             135             140
Tyr Phe Lys Ile Val Ser Ser Ile Arg Ser Met Ser Ser Val Gln Gly
      145             150             155             160
Lys Tyr Lys Ala Phe Ser Thr Cys Ala Ser His Leu Ser Ile Val Ser
      165             170             175
Leu Phe Tyr Ser Thr Gly Leu Gly Val Tyr Val Ser Ser Ala Val Ile
      180             185             190
Arg Ser Ser His Ser Ser Ala Ser Ala Ser Val Met Tyr Thr Val Val
      195             200             205
Thr Pro Met Leu
      210

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(2) INFORMATION FOR SEQ ID NO:17:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 646 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA

(iii) HYPOTHETICAL: YES

(iv) ANTI-SENSE: NO

(vi) ORIGINAL SOURCE:

- (A) ORGANISM: rat olfactory epithelium
- (B) STRAIN: erpague-Dawley rat
- (F) TISSUE TYPE: olfactory epithelium

(vii) IMMEDIATE SOURCE:

- (B) CLONE: J4

(ix) FEATURE:

- (A) NAME/KEY: CDS
- (B) LOCATION: 2..646

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:17:

C ATA GGC TAT TCA TCT TCT GTC ACA CCC AAT ATG CTT GTC AAC TTC

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Ile	Gly	Tyr	Ser	Ser	Ser	Val	Thr	Pro	Asn	Met	Leu	Val	Asn	Phe		
1				5				10					15			
CTT	ATA	AAG	CAA	AAT	ACC	ATC	TCA	TAC	CTT	GGA	TGT	TCT	ATA	CAG	TTT	94
Leu	Ile	Lys	Gln	Asn	Thr	Ile	Ser	Tyr	Leu	Gly	Cys	Ser	Ile	Gln	Phe	
			20					25					30			
GGC	TCA	GCT	GCT	TTG	TTT	GGA	GGT	CTT	GAA	TGC	TTC	CTT	CTG	GCT	GCC	142
Gly	Ser	Ala	Ala	Leu	Phe	Gly	Gly	Leu	Glu	Cys	Phe	Leu	Leu	Ala	Ala	
		35				40						45				
ATG	CGC	TAT	GAT	CGT	TTT	GTA	GCA	ATC	TGC	AAC	CCA	CTG	CTT	TAT	TCA	190
Met	Ala	Tyr	Asp	Arg	Phe	Val	Ala	Ile	Cys	Asn	Pro	Leu	Leu	Tyr	Ser	
	50					55					60					
ACG	AAA	ATG	TCC	ACA	CAA	GTC	TGT	GTC	CAG	TTG	GTT	GTG	GGA	TCT	TAT	238
Thr	Lys	Met	Ser	Thr	Gln	Val	Cys	Val	Gln	Leu	Val	Val	Gly	Ser	Tyr	
	65				70					75						
ATA	GGG	GGA	TTT	CTT	AAT	GCC	TCC	TCT	TTT	ACC	CTT	TCC	TTT	TTT	TCC	286
Ile	Gly	Gly	Phe	Leu	Asn	Ala	Ser	Ser	Phe	Thr	Leu	Ser	Phe	Phe	Ser	
	80				85				90						95	
TTG	TCC	TTC	TGT	GGA	CCA	AAT	AGA	ATC	AAT	CAC	TTT	TAC	TGT	GAT	TTT	334
Leu	Ser	Phe	Cys	Gly	Pro	Asn	Arg	Ile	Asn	His	Phe	Tyr	Cys	Asp	Phe	
			100					105					110			
GCT	CCG	TTA	GTA	GAA	CTT	TCT	TGC	TCT	GAT	GTC	AGT	GTT	CCT	GAT	GCT	382
Ala	Pro	Leu	Val	Glu	Leu	Ser	Cys	Ser	Asp	Val	Ser	Val	Pro	Asp	Ala	
		115						120					125			
GTT	ACC	TCA	TTT	TCT	GCT	GCC	TCA	GTT	ACT	ATG	CTC	ACA	GTG	TTT	ATC	430
Val	Thr	Ser	Phe	Ser	Ala	Ala	Ser	Val	Thr	Met	Leu	Thr	Val	Phe	Ile	
	130						135					140				
ATA	GCC	ATC	TCC	TAT	ACC	TAT	ATC	CTC	ATC	ACC	ATC	CTG	AAG	ATG	CGT	478
Ile	Ala	Ile	Ser	Tyr	Thr	Tyr	Ile	Leu	Ile	Thr	Ile	Leu	Lys	Met	Arg	
	145					150					155					
TCC	ACT	GAG	GGT	CGA	CAG	AAA	GCA	TTC	TCT	ACC	TGC	ACT	TCC	CAC	CTC	526
Ser	Thr	Glu	Gly	Arg	Gln	Lys	Ala	Phe	Ser	Thr	Cys	Thr	Ser	His	Leu	
	160				165					170					175	
ACT	GCA	GTC	ACT	CTG	TGC	TAT	GGA	ACC	ATC	ACA	TTC	ATC	TAT	GTG	ATG	574
Thr	Ala	Val	Thr	Leu	Cys	Tyr	Gly	Thr	Ile	Thr	Phe	Ile	Tyr	Val	Met	
			180					185					190			
CCC	AAG	TCC	AGC	TAC	TCC	ACA	GAC	CAG	AAC	AAG	GTG	GTG	TCT	GTG	TTT	622
Pro	Lys	Ser	Ser	Tyr	Ser	Thr	Asp	Gln	Asn	Lys	Val	Val	Ser	Val	Phe	
		195						200					205			
TAT	ATG	GTG	GTG	ATC	CCC	ATG	TTG									646
Tyr	Met	Val	Val	Ile	Pro	Met	Leu									
	210					215										

(2) INFORMATION FOR SEQ ID NO:18:

- (i) SEQUENCE CHARACTERISTICS:
- (A) LENGTH: 215 amino acids
 - (B) TYPE: amino acid
 - (D) TOPOLOGY: linear

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(ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:18:

```

Ile Gly Tyr Ser Ser Ser Val Thr Pro Asn Met Leu Val Asn Phe Leu
 1           5           10           15
Ile Lys Gln Asn Thr Ile Ser Tyr Leu Gly Cys Ser Ile Gln Phe Gly
          20           25           30
Ser Ala Ala Leu Phe Gly Gly Leu Glu Cys Phe Leu Leu Ala Ala Met
          35           40           45
Ala Tyr Asp Arg Phe Val Ala Ile Cys Asn Pro Leu Leu Tyr Ser Thr
          50           55           60
Lys Met Ser Thr Gln Val Cys Val Gln Leu Val Val Gly Ser Tyr Ile
          65           70           75           80
Gly Gly Phe Leu Asn Ala Ser Ser Phe Thr Leu Ser Phe Phe Ser Leu
          85           90           95
Ser Phe Cys Gly Pro Asn Arg Ile Asn His Phe Tyr Cys Asp Phe Ala
          100          105          110
Pro Leu Val Glu Leu Ser Cys Ser Asp Val Ser Val Pro Asp Ala Val
          115          120          125
Thr Ser Phe Ser Ala Ala Ser Val Thr Met Leu Thr Val Phe Ile Ile
          130          135          140
Ala Ile Ser Tyr Thr Tyr Ile Leu Ile Thr Ile Leu Lys Met Arg Ser
          145          150          155          160
Thr Glu Gly Arg Gln Lys Ala Phe Ser Thr Cys Thr Ser His Leu Thr
          165          170          175
Ala Val Thr Leu Cys Tyr Gly Thr Ile Thr Phe Ile Tyr Val Met Pro
          180          185          190
Lys Ser Ser Tyr Ser Thr Asp Gln Asn Lys Val Val Ser Val Phe Tyr
          195          200          205
Met Val Val Ile Pro Met Leu
          210          215

```

(2) INFORMATION FOR SEQ ID NO:19:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 481 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA

(iii) HYPOTHETICAL: YES

(iv) ANTI-SENSE: NO

(vi) ORIGINAL SOURCE:

- (A) ORGANISM: rat olfactory epithelium

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(B) STRAIN: Srpague-Dawley rat
(F) TISSUE TYPE: o'factory epithelium

(vii) IMMEDIATE SOURCE:
(B) CLONE: J7

(ix) FEATURE:
(A) NAME/KEY: CDS
(B) LOCATION: 2..481

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:19:

C ATC TGC AAG CCC CTG CAC TAC ACC ACC ATC ATG AAT AAC CGA GTG	46
Ile Cys Lys Pro Leu His Tyr Thr Thr Ile Met Asn Asn Arg Val	
1 5 10 15	
TGC ACA GTT CTA GTC CTC TCC TGT TGG TTT GCT GGC CTG TTG ATC ATC	94
Cys Thr Val Leu Val Leu Ser Cys Trp Phe Ala Gly Leu Leu Ile Ile	
20 25 30	
CTC CCA CCT CTT GGT CAT GGC CTC CAG CTG GAG TTC TGT GAC TCC AAT	142
Leu Pro Pro Leu Gly His Gly Leu Gln Leu Glu Phe Cys Asp Ser Asn	
35 40 45	
GTG ATT GAT CAT TTT GGC TGT GAT GCC TCT CCA ATT CTG CAG ATA ACC	190
Val Ile Asp His Phe Gly Cys Asp Ala Ser Pro Ile Leu Gln Ile Thr	
50 55 60	
TGC TCA GAC ACG GTA TTT ATA GAG AAA ATT GTC TTG GCT TTT GCC ATA	238
Cys Ser Asp Thr Val Phe Ile Glu Lys Ile Val Leu Ala Phe Ala Ile	
65 70 75	
CTG ACA CTC ATC ATT ACT CTG GTA TGT GTT GTT CTC TCC TAC ACA TAC	286
Leu Thr Leu Ile Ile Thr Leu Val Cys Val Val Leu Ser Tyr Thr Tyr	
80 85 90 95	
ATC ATC AAG ACC ATT TTA AAG TTT CCT TCT GCT CAA CAA AGA AAA AAG	334
Ile Ile Lys Thr Ile Leu Lys Phe Pro Ser Ala Gln Gln Arg Lys Lys	
100 105 110	
GCC TTT TCT ACA TGT TCT TCC CAC ATG ATT GTG GTT TCC ATC ACC TAT	382
Ala Phe Ser Thr Cys Ser Ser His Met Ile Val Val Ser Ile Thr Tyr	
115 120 125	
GGG AGC TGT ATT TTC ATC TAC ATC AAA CCT TCA GCG AAG GAA GGG GTA	430
Gly Ser Cys Ile Phe Ile Tyr Ile Lys Pro Ser Ala Lys Glu Gly Val	
130 135 140	
GCC ATC AAT AAG GTT GTA TCT GTG CTC ACA ACA TCA GTC GCC CCT TTG	478
Ala Ile Asn Lys Val Val Ser Val Leu Thr Thr Ser Val Ala Pro Leu	
145 150 155	
CTC	481
Leu	
160	

(2) INFORMATION FOR SEQ ID NO:20:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 160 amino acids

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(B) TYPE: amino acid
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:20:

```

Ile Cys Lys Pro Leu His Tyr Thr Thr Ile Met Asn Asn Arg Val Cys
 1           5           10           15
Thr Val Leu Val Leu Ser Cys Trp Phe Ala Gly Leu Leu Ile Ile Leu
          20           25           30
Pro Pro Leu Gly His Gly Leu Gln Leu Glu Phe Cys Asp Ser Asn Val
          35           40           45
Ile Asp His Phe Gly Cys Asp Ala Ser Pro Ile Leu Gln Ile Thr Cys
          50           55           60
Ser Asp Thr Val Phe Ile Glu Lys Ile Val Leu Ala Phe Ala Ile Leu
          65           70           75           80
Thr Leu Ile Ile Thr Leu Val Cys Val Val Leu Ser Tyr Thr Tyr Ile
          85           90           95
Ile Lys Thr Ile Leu Lys Phe Pro Ser Ala Gln Gln Arg Lys Lys Ala
          100           105           110
Phe Ser Thr Cys Ser Ser His Met Ile Val Val Ser Ile Thr Tyr Gly
          115           120           125
Ser Cys Ile Phe Ile Tyr Ile Lys Pro Ser Ala Lys Glu Gly Val Ala
          130           135           140
Ile Asn Lys Val Val Ser Val Leu Thr Thr Ser Val Ala Pro Leu Leu
          145           150           155           160

```

(2) INFORMATION FOR SEQ ID NO:21:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 481 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

(iii) HYPOTHETICAL: YES

(iv) ANTI-SENSE: NO

(vi) ORIGINAL SOURCE:

(A) ORGANISM: rat olfactory epithelium
(B) STRAIN: Sprague-Dawley rat
(F) TISSUE TYPE: olfactory epithelium

(vii) IMMEDIATE SOURCE:

(B) CLONE: J8

(ix) FEATURE:

(A) NAME/KEY: CDS

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(B) LOCATION: 2..481

(x1) SEQUENCE DESCRIPTION: SEQ ID NO:21:

C	ATC	TGC	CAC	CCG	CTC	CAC	TAC	TCT	CTT	CTC	ATG	AGT	CCT	GAC	AAC	46
Ile	Cys	His	Pro	Leu	His	Tyr	Ser	Leu	Leu	Met	Ser	Pro	Asp	Asn		
1				5					10					15		
TGT	GCT	GCT	CTG	GTA	ACA	GTC	TCC	TGG	GTG	ACA	GGG	GTG	GGC	ACG	GGC	94
Cys	Ala	Ala	Leu	Val	Thr	Val	Ser	Trp	Val	Thr	Gly	Val	Gly	Thr	Gly	
			20					25					30			
TTC	CTG	CCT	TCC	CTC	CTG	ATT	TCT	AAG	TTG	GAC	TTC	TGT	GGG	CCC	AAC	142
Phe	Leu	Pro	Ser	Leu	Leu	Ile	Ser	Lys	Leu	Asp	Phe	Cys	Gly	Pro	Asn	
			35					40					45			
CGC	ATC	AAC	CAT	TTC	TTC	TGT	GAC	CTC	CCT	CCA	TTA	ATC	CAG	CTG	TCC	190
Arg	Ile	Asn	His	Phe	Phe	Cys	Asp	Leu	Pro	Pro	Leu	Ile	Gln	Leu	Ser	
		50					55					60				
TGC	TCC	AGC	GTC	TTT	GTG	ACA	GAA	ATG	GCC	ATC	TTT	GTG	CTG	TCC	ATC	238
Cys	Ser	Ser	Val	Phe	Val	Thr	Glu	Met	Ala	Ile	Phe	Val	Leu	Ser	Ile	
	65					70					75					
GCT	GTG	CTC	TGC	ATC	TGT	TTC	CTC	CTA	ACC	CNN	NNN	TCC	TAC	ATT	TTC	286
Ala	Val	Leu	Cys	Ile	Cys	Phe	Leu	Leu	Thr	Xaa	Xaa	Ser	Tyr	Ile	Phe	
	80				85					90				95		
ATA	GTG	TCC	TCC	ATT	CTG	AGA	ATC	CCT	TCC	ACT	ACC	GGC	AGG	ATG	AAG	334
Ile	Val	Ser	Ser	Ile	Leu	Arg	Ile	Pro	Ser	Thr	Thr	Gly	Arg	Met	Lys	
				100				105						110		
ACA	TTT	TCT	ACA	TGT	GGC	TCC	CAC	CTG	GCC	GTG	GTC	ACC	ATC	TAC	TAT	382
Thr	Phe	Ser	Thr	Cys	Gly	Ser	His	Leu	Ala	Val	Val	Thr	Ile	Tyr	Tyr	
			115					120					125			
GGG	ACC	ATG	ATC	TCC	ATG	TAT	GTC	GCC	CCA	AAT	GCG	CAT	CTG	TCC	CCG	430
Gly	Thr	Met	Ile	Ser	Met	Tyr	Val	Gly	Pro	Asn	Ala	His	Leu	Ser	Pro	
		130					135						140			
GAG	CTC	AAC	AAG	GTC	ATT	TCT	GTC	TTC	TAC	ACT	GTG	ATC	ACC	CCA	CTA	478
Glu	Leu	Asn	Lys	Val	Ile	Ser	Val	Phe	Tyr	Thr	Val	Ile	Thr	Pro	Leu	
	145					150					155					
CTG																481
Leu																
160																

(2) INFORMATION FOR SEQ ID NO:22:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 160 amino acids

(B) TYPE: amino acid

(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:22:

Ile Cys His Pro Leu His Tyr Ser Leu Leu Met Ser Pro Asp Asn Cys

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```

      1             5             10             15
Ala Ala Leu Val Thr Val Ser Trp Val Thr Gly Val Gly Thr Gly Phe
      20             25             30
Leu Pro Ser Leu Leu Ile Ser Lys Leu Asp Phe Cys Gly Pro Asn Arg
      35             40             45
Ile Asn His Phe Phe Cys Asp Leu Pro Pro Leu Ile Gln Leu Ser Cys
      50             55             60
Ser Ser Val Phe Val Thr Glu Met Ala Ile Phe Val Leu Ser Ile Ala
      65             70             75             80
Val Leu Cys Ile Cys Phe Leu Leu Thr Xaa Xaa Ser Tyr Ile Phe Ile
      85             90             95
Val Ser Ser Ile Leu Arg Ile Pro Ser Thr Thr Gly Arg Met Lys Thr
      100            105            110
Phe Ser Thr Cys Gly Ser His Leu Ala Val Val Thr Ile Tyr Tyr Gly
      115            120            125
Thr Met Ile Ser Met Tyr Val Gly Pro Asn Ala His Leu Ser Pro Glu
      130            135            140
Leu Asn Lys Val Ile Ser Val Phe Tyr Thr Val Ile Thr Pro Leu Leu
      145            150            155            160

```

(2) INFORMATION FOR SEQ ID NO:23:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 646 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

(iii) HYPOTHETICAL: YES

(iv) ANTI-SENSE: NO

(vi) ORIGINAL SOURCE:

- (A) ORGANISM: rat olfactory epithelium
- (B) STRAIN: Sprague-Dawley rat
- (F) TISSUE TYPE: olfactory epithelium

(vii) IMMEDIATE SOURCE:

- (B) CLONE: J11

(ix) FEATURE:

- (A) NAME/KEY: CDS
- (B) LOCATION: 2..646

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:23:

```

N GTC TGC TTC TCC TCC ACC ACT GTC CCC AAG GTA CTG GCT AAC CAC
  Val Cys Phe Ser Ser Thr Thr Val Pro Lys Val Leu Ala Asn His
    1             5             10             15

```

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ATA CTC AGT AGT CAG GCC ATT TCC TTC TCT GGG TGT CTA ACT CAG CTG Ile Leu Ser Ser Gln Ala Ile Ser Phe Ser Gly Cys Leu Thr Gln Leu 20 25 30	94
TAT TTT CTC TGT GTG TCT GTG AAT ATG GAC AAT TTC CTG CTG GCT GTG Tyr Phe Leu Cys Val Ser Val Asn Met Asp Asn Phe Leu Leu Ala Val 35 40 45	142
ATG GCC TAT GAC AGA TTT GTG GCC ATA TGC CAC CCT TTG TAC TAC ACA Met Ala Tyr Asp Arg Phe Val Ala Ile Cys His Pro Leu Tyr Tyr Thr 50 55 60	190
ACA AAG ATG ACC CAC CAG CTC TGT GTC TTG CTG GTG TCT GGA TCA NNN Thr Lys Met Thr His Gln Leu Cys Val Leu Leu Val Ser Gly Ser Xaa 65 70 75	238
NNN NNN NNN NNN NNN NNN NNN NNN NNN NNN NNN NNN NNN NNN NNN Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa 80 85 90 95	286
NNN NNN NNN NNN NNN NNN NNN NNN NNN NNN NNN NNN NNN NNN NNN Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa 100 105 110	334
NNN NNN NNN NNN NNN NNN NNN NNN NNN NNN NNN NNN NNN NNN NNN Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa 115 120 125	382
NNN NNN NNN NNN NNN NNN NNT GTG ATC ATG GTC ACC CCA TTT GTC TGC Xaa Xaa Xaa Xaa Xaa Xaa Xaa Val Ile Met Val Thr Pro Phe Val Cys 130 135 140	430
ATC CTC ATC TCT TAC ATC TAC ATC ACC AAT GCA GTC CTC AGA GTC TCA Ile Leu Ile Ser Tyr Ile Tyr Ile Thr Asn Ala Val Leu Arg Val Ser 145 150 155	478
TCC TTT AGG GGA GGA TGG AAA GCC TTC TCC ACC TGT GGC TCA CAC CTG Ser Phe Arg Gly Gly Trp Lys Ala Phe Ser Thr Cys Gly Ser His Leu 160 165 170 175	526
GCT GTG GTC TGC CTC TTC TAT GGC ACC ATC ATT GCT GTG TAT TTC AAT Ala Val Val Cys Leu Phe Tyr Gly Thr Ile Ile Ala Val Tyr Phe Asn 180 185 190	574
CCT GTA TCT TCC CAT TCA TCT GAG AAG GAC ACT GCA GCA ACT GTG CTA Pro Val Ser Ser His Ser Ser Glu Lys Asp Thr Ala Ala Thr Val Leu 195 200 205	622
TAC ACA GTG GTG ACT CCC ATG TTG Tyr Thr Val Val Thr Pro Met Leu 210 215	646

(2) INFORMATION FOR SEQ ID NO:24:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 215 amino acids
- (B) TYPE: amino acid
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

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(xi) SEQUENCE DESCRIPTION: SEQ ID NO:24:

```

Val Cys Phe Ser Ser Thr Thr Val Pro Lys Val Leu Ala Asn His Ile
 1           5           10           15
Leu Ser Ser Gln Ala Ile Ser Phe Ser Gly Cys Leu Thr Gln Leu Tyr
 20           25           30
Phe Leu Cys Val Ser Val Asn Met Asp Asn Phe Leu Leu Ala Val Met
 35           40           45
Ala Tyr Asp Arg Phe Val Ala Ile Cys His Pro Leu Tyr Tyr Thr Thr
 50           55           60
Lys Met Thr His Gln Leu Cys Val Leu Leu Val Ser Gly Ser Xaa Xaa
 65           70           75           80
Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa
 85           90           95
Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa
100          105          110
Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa
115          120          125
Xaa Xaa Xaa Xaa Xaa Xaa Val Ile Met Val Thr Pro Phe Val Cys Ile
130          135          140
Leu Ile Ser Tyr Ile Tyr Ile Thr Asn Ala Val Leu Arg Val Ser Ser
145          150          155          160
Phe Arg Gly Gly Trp Lys Ala Phe Ser Thr Cys Gly Ser His Leu Ala
165          170          175
Val Val Cys Leu Phe Tyr Gly Thr Ile Ile Ala Val Tyr Phe Asn Pro
180          185          190
Val Ser Ser His Ser Ser Glu Lys Asp Thr Ala Ala Thr Val Leu Tyr
195          200          205
Thr Val Val Thr Pro Met Leu
210          215

```

(2) INFORMATION FOR SEQ ID NO:25:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 646 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA

(iii) HYPOTHETICAL: YES

(iv) ANTI-SENSE: NO

(vi) ORIGINAL SOURCE:

- (A) ORGANISM: rat olfactory epithelium
- (B) STRAIN: Sprague-Dawley rat
- (F) TISSUE TYPE: olfactory epithelium

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(vii) IMMEDIATE SOURCE:
(B) CLONE: J14

(ix) FEATURE:
(A) NAME/KEY: CDS
(B) LOCATION: 2..646

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:25:

T GTC TGC TTC TCC TCC ACC ACT GTC CCC AAG GTA CTG GCT AAC CAC	46
Val Cys Phe Ser Ser Thr Thr Val Pro Lys Val Leu Ala Asn His	
1 5 10 15	
ATA CTC AGT AGT CAG GCC ATT TCC TTC TCT GGG TGT CTA ACT CAG CTG	94
Ile Leu Ser Ser Gln Ala Ile Ser Phe Ser Gly Cys Leu Thr Gln Leu	
20 25 30	
TAT TTT CTC TGT GTG TCT GTG AAT ATG GAC AAT TTC CTG CTG GCT GTG	142
Tyr Phe Leu Cys Val Ser Val Asn Met Asp Asn Phe Leu Leu Ala Val	
35 40 45	
ATG GCC TAT GAC AGA TTT GTG GCC ATA TGC CAC CCT TTG TAC TAC ACA	190
Met Ala Tyr Asp Arg Phe Val Ala Ile Cys His Pro Leu Tyr Tyr Thr	
50 55 60	
ACA CCG ATG ACC CAC CAG CTC TGT GTC TTG CTG GTG TCT GGA TCA NNN	238
Thr Pro Met Thr His Gln Leu Cys Val Leu Leu Val Ser Gly Ser Xaa	
65 70 75	
NNN NNN NNN NNN NNN NNN NNN NNN NNN NNN NNN NNN NNN NNN NNN	286
Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa	
80 85 90 95	
NNN NNN NNN NNN NNN NNN NNN NNN NNN NNN NNN NNN NNN NNN NNN	334
Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa	
100 105 110	
NNN NNN NNN NNN NNN NNN NNN NNN NNN NNN NNN NNN NNN NNN NNN	382
Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa	
115 120 125	
NNN NNN NNN NNN NNN NNN NNT GTG ATC ATG GTC ACC CCA TTT GTC TGC	430
Xaa Xaa Xaa Xaa Xaa Xaa Xaa Val Ile Met Val Thr Pro Phe Val Cys	
130 135 140	
ATC CTC ATC TCT TAC ATC TAC ATC ACC AAT GCA GTC CTC AGA GTC TCA	478
Ile Leu Ile Ser Tyr Ile Tyr Ile Thr Asn Ala Val Leu Arg Val Ser	
145 150 155	
TCC TTT AGG GGA GGA TGG AAA GCC TTC TCC ACC TGT GGC TCA CAC CTG	526
Ser Phe Arg Gly Gly Trp Lys Ala Phe Ser Thr Cys Gly Ser His Leu	
160 165 170 175	
GCT GTG GTC TGC CTC TTC TAT GGC ACC ATC ATT GCT GTG TAT TTC AAT	574
Ala Val Val Cys Leu Phe Tyr Gly Thr Ile Ile Ala Val Tyr Phe Asn	
180 185 190	
CCT GTA TCT TCC CAT TCA TCT GAG AAG GAC ACT GCA GCA ACT GTG CTA	622
Pro Val Ser Ser His Ser Ser Glu Lys Asp Thr Ala Ala Thr Val Leu	
195 200 205	

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TAC ACA GTG GTG ACT CCC ATG TTG
 Tyr Thr Val Val Thr Pro Met Leu
 210 215

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(2) INFORMATION FOR SEQ ID NO:26:

(1) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 215 amino acids
 (B) TYPE: amino acid
 (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:26:

Val Cys Phe Ser Ser Thr Thr Val Pro Lys Val Leu Ala Asn His Ile
 1 5 10 15
 Leu Ser Ser Gln Ala Ile Ser Phe Ser Gly Cys Leu Thr Gln Leu Tyr
 20 25 30
 Phe Leu Cys Val Ser Val Asn Met Asp Asn Phe Leu Leu Ala Val Met
 35 40 45
 Ala Tyr Asp Arg Phe Val Ala Ile Cys His Pro Leu Tyr Tyr Thr Thr
 50 55 60
 Pro Met Thr His Gln Leu Cys Val Leu Leu Val Ser Gly Ser Xaa Xaa
 65 70 75 80
 Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa
 85 90 95
 Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa
 100 105 110
 Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa
 115 120 125
 Xaa Xaa Xaa Xaa Xaa Xaa Val Ile Met Val Thr Pro Phe Val Cys Ile
 130 135 140
 Leu Ile Ser Tyr Ile Tyr Ile Thr Asn Ala Val Leu Arg Val Ser Ser
 145 150 155 160
 Phe Arg Gly Gly Trp Lys Ala Phe Ser Thr Cys Gly Ser His Leu Ala
 165 170 175
 Val Val Cys Leu Phe Tyr Gly Thr Ile Ile Ala Val Tyr Phe Asn Pro
 180 185 190
 Val Ser Ser His Ser Ser Glu Lys Asp Thr Ala Ala Thr Val Leu Tyr
 195 200 205
 Thr Val Val Thr Pro Met Leu
 210 215

(2) INFORMATION FOR SEQ ID NO:27:

(1) SEQUENCE CHARACTERISTICS:

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(A) LENGTH: 481 base pairs
 (B) TYPE: nucleic acid
 (C) STRANDEDNESS: single
 (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA

(iii) HYPOTHETICAL: YES

(iv) ANTI-SENSE: NO

(vi) ORIGINAL SOURCE:

(A) ORGANISM: rat olfactory epithelium
 (B) STRAIN: Sprague-Dawley rat
 (F) TISSUE TYPE: olfactory epithelium

(vii) IMMEDIATE SOURCE:

(B) CLONE: J15

(ix) FEATURE:

(A) NAME/KEY: CDS
 (B) LOCATION: 2..481

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:27:

T ATC TGC AAC CCT CTG CGC TAC CCA GTG CTC ATG AGC GGC CGG CTG	46
Ile Cys Asn Pro Leu Arg Tyr Pro Val Leu Met Ser Gly Arg Val	
1 5 10 15	
TGC CTG CTC ATG GTC GTG GCC TCC TCG TTG GGA GGA TCC CTC AAC GCC	94
Cys Leu Leu Met Val Val Ala Ser Trp Leu Gly Gly Ser Leu Asn Ala	
20 25 30	
TCC ATT CAG ACT TCT CTG ACC CTT CAG TTC CCC TAC TGT GGA TCA CGG	142
Ser Ile Gln Thr Ser Leu Thr Leu Gln Phe Pro Tyr Cys Gly Ser Arg	
35 40 45	
AAG ATC TCC CAC TTC TTC TGT GAG GTG CCC TCG CTG CTG ANN NTG GCC	190
Lys Ile Ser His Phe Phe Cys Glu Val Pro Ser Leu Leu Xaa Xaa Ala	
50 55 60	
TGT GCA GAC ACT GAA GCC TAT GAG CAG GTA CTA TTT GTG ACA GGC GTG	238
Cys Ala Asp Thr Glu Ala Tyr Glu Gln Val Leu Phe Val Thr Gly Val	
65 70 75	
GTG GTC CTC CTG GTG CCC ATT ACA TTC ATT ACT GCC TCT TAT GCC CTC	286
Val Val Leu Leu Val Pro Ile Thr Phe Ile Thr Ala Ser Tyr Ala Leu	
80 85 90 95	
ATC CTG GCT GCT GTG CTC CGA ATG CAC TCT GCG GAG GGG AGT CAG AAG	334
Ile Leu Ala Ala Val Leu Arg Met His Ser Ala Glu Gly Ser Gln Lys	
100 105 110	
GCC CTA GCC ACA TGC TCC TCT CAC CTG ACA GTC GTC AAT CTC TTC TAT	382
Ala Leu Ala Thr Cys Ser Ser His Leu Thr Val Val Asn Leu Phe Tyr	
115 120 125	
GGG CCC CTT GTC TAC ACC TAC ATG TTA CCT GCT TCC TAT CAC TCA CCA	430
Gly Pro Leu Val Tyr Thr Tyr Met Leu Pro Ala Ser Tyr His Ser Pro	
130 135 140	

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GGC CAA GAC GAC ATA GTA TCC GTC TTT TAC ACC GTT CTC ACA CCC ATG 478
 Gly Gln Asp Asp Ile Val Ser Val Phe Tyr Thr Val Leu Thr Pro Met
 145 150 155

CTT 481
 Leu
 160

(2) INFORMATION FOR SEQ ID NO:28:

- (i) SEQUENCE CHARACTERISTICS:
 (A) LENGTH: 160 amino acids
 (B) TYPE: amino acid
 (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:28:

Ile Cys Asn Pro Leu Arg Tyr Pro Val Leu Met Ser Gly Arg Val Cys
 1 5 10 15
 Leu Leu Met Val Val Ala Ser Trp Leu Gly Gly Ser Leu Asn Ala Ser
 20 25 30
 Ile Gln Thr Ser Leu Thr Leu Gln Phe Pro Tyr Cys Gly Ser Arg Lys
 35 40 45
 Ile Ser His Phe Phe Cys Glu Val Pro Ser Leu Leu Xaa Xaa Ala Cys
 50 55 60
 Ala Asp Thr Glu Ala Tyr Glu Gln Val Leu Phe Val Thr Gly Val Val
 65 70 75 80
 Val Leu Leu Val Pro Ile Thr Phe Ile Thr Ala Ser Tyr Ala Leu Ile
 85 90 95
 Leu Ala Ala Val Leu Arg Met His Ser Ala Glu Gly Ser Gln Lys Ala
 100 105 110
 Leu Ala Thr Cys Ser Ser His Leu Thr Val Val Asn Leu Phe Tyr Gly
 115 120 125
 Pro Leu Val Tyr Thr Tyr Met Leu Pro Ala Ser Tyr His Ser Pro Gly
 130 135 140
 Gln Asp Asp Ile Val Ser Val Phe Tyr Thr Val Leu Thr Pro Met Leu
 145 150 155 160

(2) INFORMATION FOR SEQ ID NO:29:

- (i) SEQUENCE CHARACTERISTICS:
 (A) LENGTH: 481 base pairs
 (B) TYPE: nucleic acid
 (C) STRANDEDNESS: single
 (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA

(iii) HYPOTHETICAL: YES

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(iv) ANTI-SENSE: NO

(vi) ORIGINAL SOURCE:

(A) ORGANISM: rat olfactory epithelium

(B) STRAIN: Sprague-Dawley rat

(F) TISSUE TYPE: olfactory epithelium

(vii) IMMEDIATE SOURCE:

(B) CLONE: J16

(ix) FEATURE:

(A) NAME/KEY: CDS

(B) LOCATION: 2..481

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:29:

C ATC TGT AGG CCT CTT CAC TAT CCT ACC CTC ATG ACC CAG ACA CTG	46
Ile Cys Arg Pro Leu His Tyr Pro Thr Leu Met Thr Gln Thr Leu	
1 5 10 15	
TGT GCC AAG ATT GCC ACT GGT TGC TGG TTG GGA GGC TTG GCT GGG CCA	94
Cys Ala Lys Ile Ala Thr Gly Cys Trp Leu Gly Gly Leu Ala Gly Pro	
20 25 30	
GTG GTA GAA ATT TCC TTG GTG TCT CGT CTC CTT TTT TGT GGC CCC AAT	142
Val Val Glu Ile Ser Leu Val Ser Arg Leu Leu Phe Cys Gly Pro Asn	
35 40 45	
CAC ATT CAA CAC ATC TTT TGT GAT TTC CCA CCT GTG CTG AGC TTG GCT	190
His Ile Gln His Ile Phe Cys Asp Phe Pro Pro Val Leu Ser Leu Ala	
50 55 60	
TGT ACT GAT ACA TCA GTG AAT GTC CTG CTA GAT TTT ATT ATA AAC CTC	238
Cys Thr Asp Thr Ser Val Asn Val Leu Val Asp Phe Ile Ile Asn Leu	
65 70 75	
TGC AAG ATC CTG GCC ACC TTC CTG CTG ATC CTG AGC TCC TAC TTG CAG	286
Cys Lys Ile Leu Ala Thr Phe Leu Leu Ile Leu Ser Ser Tyr Leu Gln	
80 85 90 95	
ATA ATC CGC ACA GTG CTC AAG ATT CCT TCA GCT GCA GGC AAG AAG AAA	334
Ile Ile Arg Thr Val Leu Lys Ile Pro Ser Ala Ala Gly Lys Lys Lys	
100 105 110	
GCA TTC TCG ACT TGT GCC TCC CAT CTC ACT GTG GTT CTC ATC TTC TAT	382
Ala Phe Ser Thr Cys Ala Ser His Leu Thr Val Val Leu Ile Phe Tyr	
115 120 125	
GGG AGC ATC CTT TTC ATG TAT GTG CGG CTG AAG AAG ACT TAC TCC CTT	430
Gly Ser Ile Leu Phe Met Tyr Val Arg Leu Lys Lys Thr Tyr Ser Leu	
130 135 140	
GAC TAC GAC AGA GCC TTG GCA GTA GTC TAC TCC GTG GTT ACC CCT TTC	478
Asp Tyr Asp Arg Ala Leu Ala Val Val Tyr Ser Val Val Thr Pro Phe	
145 150 155	
CTG	481
Leu	
160	

(2) INFORMATION FOR SEQ ID NO:30:

-79-

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 160 amino acids
- (B) TYPE: amino acid
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:30:

```

Ile Cys Arg Pro Leu His Tyr Pro Thr Leu Met Thr Gln Thr Leu Cys
 1           5           10           15
Ala Lys Ile Ala Thr Gly Cys Trp Leu Gly Gly Leu Ala Gly Pro Val
          20           25           30
Val Glu Ile Ser Leu Val Ser Arg Leu Leu Phe Cys Gly Pro Asn His
          35           40           45
Ile Gln His Ile Phe Cys Asp Phe Pro Pro Val Leu Ser Leu Ala Cys
          50           55           60
Thr Asp Thr Ser Val Asn Val Leu Val Asp Phe Ile Ile Asn Leu Cys
          65           70           75           80
Lys Ile Leu Ala Thr Phe Leu Leu Ile Leu Ser Ser Tyr Leu Gln Ile
          85           90           95
Ile Arg Thr Val Leu Lys Ile Pro Ser Ala Ala Gly Lys Lys Lys Ala
          100          105          110
Phe Ser Thr Cys Ala Ser His Leu Thr Val Val Leu Ile Phe Tyr Gly
          115          120          125
Ser Ile Leu Phe Met Tyr Val Arg Leu Lys Lys Thr Tyr Ser Leu Asp
          130          135          140
Tyr Asp Arg Ala Leu Ala Val Val Tyr Ser Val Val Thr Pro Phe Leu
          145          150          155          160

```

(2) INFORMATION FOR SEQ ID NO:31:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 481 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA

(iii) HYPOTHETICAL: YES

(iv) ANTI-SENSE: NO

(vi) ORIGINAL SOURCE:

- (A) ORGANISM: rat olfactory epithelium
- (B) STRAIN: Sprague-Dawley rat
- (F) TISSUE TYPE: olfactory epithelium

(vii) IMMEDIATE SOURCE:

- (B) CLONE: J17

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(ix) FEATURE:

(A) NAME/KEY: CDS

(B) LOCATION: 2..481

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:31:

A ATC TGC AAC CCA CTG CTT TAT TCC ACC AAA ATG TCC ACA CAA GTC Ile Cys Asn Pro Leu Leu Tyr Ser Thr Lys Met Ser Thr Gln Val 1 5 10 15	46
TGT ATC CAG TTG GTT GCA GGA TCT TAT ATA GGG GGT TTT CTT AAT ACT Cys Ile Gln Leu Val Ala Gly Ser Tyr Ile Gly Gly Phe Leu Asn Thr 20 25 30	94
TGC CTC ATC ATG TTT TAC TTT TTC TCT TTT CTC TTC TGT GGG CCA AAT Cys Leu Ile Met Phe Tyr Phe Phe Ser Phe Leu Phe Cys Gly Pro Asn 35 40 45	142
ATA GTT GAT CAT TTT TTC TGT GAT TTT GCT CCT TTN NTG GAA CTT TCG Ile Val Asp His Phe Phe Cys Asp Phe Ala Pro Xaa Xaa Glu Leu Ser 50 55 60	190
TGC TCT GAT GTG AGT GTC TCT GTA GTT GTT ATG TCA TTT TCT GCT GGC Cys Ser Asp Val Ser Val Ser Val Val Val Met Ser Phe Ser Ala Gly 65 70 75	238
TCA GTT ACT ATG ATC ACA GTG TTT ATC ATA GCC ATC TCC TAT TCT TAC Ser Val Thr Met Ile Thr Val Phe Ile Ile Ala Ile Ser Tyr Ser Tyr 80 85 90 95	286
ATC CTC ATC ACC ATC CTG AAG ATG TCC TCA ACT GAG GGC CGT CAC AAG Ile Leu Ile Thr Ile Leu Lys Met Ser Ser Thr Glu Gly Arg His Lys 100 105 110	334
GCT TTC TCC ACA TGT ACC TCC CAC CTC ACT GCA GTC ACT CTC TAC TAT Ala Phe Ser Thr Cys Thr Ser His Leu Thr Ala Val Thr Leu Tyr Tyr 115 120 125	382
GGC ACC ATT ACC TTC ATT TAT GTG ATG CCC AAG TCC ACA TAC TCT ACA Gly Thr Ile Thr Phe Ile Tyr Val Met Pro Lys Ser Thr Tyr Ser Thr 130 135 140	430
GAC CAG AAC AAG GTG GTG TCT GTG TTT TAC ATG GTG GTG ATC CCA ATG Asp Gln Asn Lys Val Val Ser Val Phe Tyr Met Val Val Ile Pro Met 145 150 155	478
TTG Leu 160	481

(2) INFORMATION FOR SEQ ID NO:32:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 160 amino acids

(B) TYPE: amino acid

(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:32:

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Ile Cys Asn Pro Leu Leu Tyr Ser Thr Lys Met Ser Thr Gln Val Cys
 1           5           10           15
Ile Gln Leu Val Ala Gly Ser Tyr Ile Gly Gly Phe Leu Asn Thr Cys
           20           25           30
Leu Ile Met Phe Tyr Phe Phe Ser Phe Leu Phe Cys Gly Pro Asn Ile
           35           40           45
Val Asp His Phe Phe Cys Asp Phe Ala Pro Xaa Xaa Glu Leu Ser Cys
           50           55           60
Ser Asp Val Ser Val Ser Val Val Val Met Ser Phe Ser Ala Gly Ser
           65           70           75           80
Val Thr Met Ile Thr Val Phe Ile Ile Ala Ile Ser Tyr Ser Tyr Ile
           85           90           95
Leu Ile Thr Ile Leu Lys Met Ser Ser Thr Glu Gly Arg His Lys Ala
           100          105          110
Phe Ser Thr Cys Thr Ser His Leu Thr Ala Val Thr Leu Tyr Tyr Gly
           115          120          125
Thr Ile Thr Phe Ile Tyr Val Met Pro Lys Ser Thr Tyr Ser Thr Asp
           130          135          140
Gln Asn Lys Val Val Ser Val Phe Tyr Met Val Val Ile Pro Met Leu
           145          150          155          160

```

(2) INFORMATION FOR SEQ ID NO:33:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 479 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA

(iii) HYPOTHETICAL: YES

(iv) ANTI-SENSE: NO

(vi) ORIGINAL SOURCE:

- (A) ORGANISM: rat olfactory epithelium
- (B) STRAIN: Sprague-Dawley rat
- (F) TISSUE TYPE: olfactory epithelium

(vii) IMMEDIATE SOURCE:

- (B) CLONE: J19

(ix) FEATURE:

- (A) NAME/KEY: CDS
- (B) LOCATION: 2..479

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:33:

```

T ATC TGC CAC CCT CTG AAG TAC ACA GTT ATC ATG AAT CAC TAT TTT
Ile Cys His Pro Leu Lys Tyr Thr Val Ile Met Asn His Tyr Phe

```

46

1	5	10	15	
TGT GTG ATG CTG CTG CTC TTC TCT GTG TTC GTT AGC ATT GCA CAT GCG				94
Cys Val Met Leu Leu Phe Ser Val Phe Val Ser Ile Ala His Ala	20	25	30	
TTG TTC CAC ATT TTA ATG GTG TTG ATA CTG ACT TTC AGC ACA AAA ACT				142
Leu Phe His Ile Leu Met Val Leu Ile Leu Thr Phe Ser Thr Lys Thr	35	40	45	
GAA ATC CCT CAC TTT TTC TGT GAG CTG GCT CAT ATC ATC AAA CTT ACC				190
Glu Ile Pro His Phe Phe Cys Glu Leu Ala His Ile Ile Lys Leu Thr	50	55	60	
TGT TCC GAT AAT TTT ATC AAC TAT CTG CTG ATA TAC ACA GAG TCT GTC				238
Cys Ser Asp Asn Phe Ile Asn Tyr Leu Leu Ile Tyr Thr Glu Ser Val	65	70	75	
TTA TTT TTT GGT GTT CAT ATT GTA GGG ATC ATT TTG TCT TAT ATT TAC				286
Leu Phe Phe Gly Val His Ile Val Gly Ile Ile Leu Ser Tyr Ile Tyr	80	85	90	95
ACT GTA TCC TCA GTT TTA AGA ATG TCA TTA TTG GGA GGA ATG TAT AAA				334
Thr Val Ser Ser Val Leu Arg Met Ser Leu Leu Gly Gly Met Tyr Lys	100	105	110	
GCC TTT TCA ACA TGT GGA TCT CAT TTG TCG GTT GTC TCT GTT TTA TGG				382
Ala Phe Ser Thr Cys Gly Ser His Leu Ser Val Val Ser Val Leu Trp	115	120	125	
CAC AGG TTT TGG GGT ACA CAT AAG CTC TCC ACT TAC TGA CTC TCC AAG				430
His Arg Phe Trp Gly Thr His Lys Leu Ser Thr Tyr * Leu Ser Lys	130	135	140	
GAA GAC TGT AGT GGC TTC AGT GAT GTA CAC TGT GGT TAC TCA GAT GCT G				479
Glu Asp Cys Ser Gly Phe Ser Asp Val His Cys Gly Tyr Ser Asp Ala	145	150	155	

(2) INFORMATION FOR SEQ ID NO:34:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 159 amino acids
- (B) TYPE: amino acid
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:34:

Ile Cys His Pro Leu Lys Tyr Thr Val Ile Met Asn His Tyr Phe Cys
 1 5 10 15
 Val Met Leu Leu Leu Phe Ser Val Phe Val Ser Ile Ala His Ala Leu
 20 25 30
 Phe His Ile Leu Met Val Leu Ile Leu Thr Phe Ser Thr Lys Thr Glu
 35 40 45
 Ile Pro His Phe Phe Cys Glu Leu Ala His Ile Ile Lys Leu Thr Cys
 50 55 60

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Ser Asp Asn Phe Ile Asn Tyr Leu Leu Ile Tyr Thr Glu Ser Val Leu
 65 70 75 80
 Phe Phe Gly Val His Ile Val Gly Ile Ile Leu Ser Tyr Ile Tyr Thr
 85 90 95
 Val Ser Ser Val Leu Arg Met Ser Leu Leu Gly Gly Met Tyr Lys Ala
 100 105 110
 Phe Ser Thr Cys Gly Ser His Leu Ser Val Val Ser Val Leu Trp His
 115 120 125
 Arg Phe Trp Gly Thr His Lys Leu Ser Thr Tyr * Leu Ser Lys Glu
 130 135 140
 Asp Cys Ser Gly Phe Ser Asp Val His Cys Gly Tyr Ser Asp Ala
 145 150 155

(2) INFORMATION FOR SEQ ID NO:35:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 481 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA

(iii) HYPOTHETICAL: YES

(iv) ANTI-SENSE: NO

(vi) ORIGINAL SOURCE:

- (A) ORGANISM: rat olfactory epithelium
- (B) STRAIN: Sprague-Dawley rat
- (F) TISSUE TYPE: olfactory epithelium

(vii) IMMEDIATE SOURCE:

- (B) CLONE: J20

(ix) FEATURE:

- (A) NAME/KEY: CDS
- (B) LOCATION: 2..481

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:35:

A ATC TGC TAC CCA CTG AGG TAC CTT CTC ATC ATG AGC TGG GTG GTG Ile Cys Tyr Pro Leu Arg Tyr Leu Leu Ile Met Ser Trp Val Val 1 5 10 15	46
TGC ACA GCA CTG TCC GTG GCA ATC TGG GTC ATA GGC TTT TGT GCC TCC Cys Thr Ala Leu Ser Val Ala Ile Trp Val Ile Gly Phe Cys Ala Ser 20 25 30	94
GTT ATA CCT CTC TGC TTC ACG ATC CTC CCA CTC TGT GGT CCT TAC GTC Val Ile Pro Leu Cys Phe Thr Ile Leu Pro Leu Cys Gly Pro Tyr Val 35 40 45	142
GTT GAT TAT CTT TTC TGC GAG CTG CCC ATC CTT CTG CAC CTG TTC TGC Val Asp Tyr Leu Phe Cys Glu Leu Pro Ile Leu Leu His Leu Phe Cys 50 55 60	190
ACA GAT ACA TCT CTG CTG GAG NNN NNN NNN NNN NNN NNN NNN NNN Thr Asp Thr Ser Leu Leu Glu Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa 65 70 75	238

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NNN NNN NNN NNN NNN CCC TTC CTC CTG ATT GTT CTC TCC TAC CTT CGC	286
Xaa Xaa Xaa Xaa Xaa Pro Phe Leu Leu Ile Val Leu Ser Tyr Leu Arg	
80 85 90 95	
ATC CTG GTG GCT GTG ATA AGA ATA GAC TCA GCT GAG GGC AGA AAA AAG	334
Ile Leu Val Ala Val Ile Arg Ile Asp Ser Ala Glu Gly Arg Lys Lys	
100 105 110	
GCC TTT TCA ACT TGT GCT TCA CAC TTG GCT GTG GTG ACC ATC TAC TAT	382
Ala Phe Ser Thr Cys Ala Ser His Leu Ala Val Val Thr Ile Tyr Tyr	
115 120 125	
GGA ACA GGG CTG ATC AGG TAC TTG AGG CCC AAG TCC CTT TAT TCC GCT	430
Gly Thr Gly Leu Ile Arg Tyr Leu Arg Pro Lys Ser Leu Tyr Ser Ala	
130 135 140	
GAG GGA GAC AGA CTG ATC TCT GTG TTC TAT GCA GTC ATT GGC CCT GCA	478
Glu Gly Asp Arg Leu Ile Ser Val Phe Tyr Ala Val Ile Gly Pro Ala	
145 150 155	
CTG	481
Leu	
160	

(2) INFORMATION FOR SEQ ID NO:36:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 160 amino acids
- (B) TYPE: amino acid
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:36:

Ile Cys Tyr Pro Leu Arg Tyr Leu Leu Ile Met Ser Trp Val Val Cys	
1 5 10 15	
Thr Ala Leu Ser Val Ala Ile Trp Val Ile Gly Phe Cys Ala Ser Val	
20 25 30	
Ile Pro Leu Cys Phe Thr Ile Leu Pro Leu Cys Gly Pro Tyr Val Val	
35 40 45	
Asp Tyr Leu Phe Cys Glu Leu Pro Ile Leu Leu His Leu Phe Cys Thr	
50 55 60	
Asp Thr Ser Leu Leu Glu Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa	
65 70 75 80	
Xaa Xaa Xaa Xaa Pro Phe Leu Leu Ile Val Leu Ser Tyr Leu Arg Ile	
85 90 95	
Leu Val Ala Val Ile Arg Ile Asp Ser Ala Glu Gly Arg Lys Lys Ala	
100 105 110	
Phe Ser Thr Cys Ala Ser His Leu Ala Val Val Thr Ile Tyr Tyr Gly	
115 120 125	
Thr Gly Leu Ile Arg Tyr Leu Arg Pro Lys Ser Leu Tyr Ser Ala Glu	
130 135 140	
Gly Asp Arg Leu Ile Ser Val Phe Tyr Ala Val Ile Gly Pro Ala Leu	
145 150 155 160	

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What is claimed is:

1. An isolated nucleic acid molecule encoding an odorant receptor.
- 5 2. An isolated DNA of claim 1.
3. An isolated cDNA of claim 2.
- 10 4. An isolated cDNA of claim 3 wherein the sequence of the cDNA has the nucleotide sequence shown in Figure 9.
5. An isolated cDNA of claim 3 wherein the sequence of the cDNA has the nucleotide sequence shown in Figure 10.
- 15 6. An isolated cDNA of claim 3 wherein the sequence of the cDNA has the nucleotide sequence shown in Figure 11.
7. An isolated cDNA of claim 3 wherein the sequence of the cDNA has the nucleotide sequence shown in Figure 12.
- 20 8. An isolated cDNA of claim 3 wherein the sequence of the cDNA has the nucleotide sequence shown in Figure 13.
- 25 9. An isolated cDNA of claim 3 wherein the sequence of the cDNA has the nucleotide sequence shown in Figure 14.
10. An isolated cDNA of claim 3 wherein the sequence of the cDNA has the nucleotide sequence shown in Figure 15.
- 30 11. An isolated cDNA of claim 3 wherein the sequence of the cDNA has the nucleotide sequence shown in Figure 16.
12. An isolated cDNA of claim 3 wherein the sequence of the cDNA has the nucleotide sequence shown in Figure 17.
- 35

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13. An isolated cDNA of claim 3 wherein the sequence of the cDNA has the nucleotide sequence shown in Figure 18.
14. An isolated cDNA of claim 3 wherein the sequence of the cDNA has the nucleotide sequence shown in Figure 19.
15. An isolated cDNA of claim 3 wherein the sequence of the cDNA has the nucleotide sequence shown in Figure 20.
16. An isolated cDNA of claim 3 wherein the sequence of the cDNA has the nucleotide sequence shown in Figure 21.
17. An isolated cDNA of claim 3 wherein the sequence of the cDNA has the nucleotide sequence shown in Figure 22.
18. An isolated cDNA of claim 3 wherein the sequence of the cDNA has the nucleotide sequence shown in Figure 23.
19. An isolated cDNA of claim 3 wherein the sequence of the cDNA has the nucleotide sequence shown in Figure 24.
20. An isolated cDNA of claim 3 wherein the sequence of the cDNA has the nucleotide sequence shown in Figure 25.
21. An isolated cDNA of claim 3 wherein the sequence of the cDNA has the nucleotide sequence shown in Figure 26.
22. An isolated cDNA of claim 3 wherein the sequence of the cDNA has the nucleotide sequence shown in Figure 27.
23. An isolated cDNA of claim 3 wherein the sequence of the cDNA has the nucleotide sequence shown in Figure 28.
24. An isolated cDNA of claim 3 wherein the sequence of the cDNA has the nucleotide sequence shown in Figure 29.

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25. An isolated cDNA of claim 3 wherein the sequence of the cDNA has the nucleotide sequence shown in Figure 30.
26. An isolated cDNA of claim 3 wherein the sequence of the cDNA has the nucleotide sequence shown in Figure 31.
27. An isolated cDNA of claim 3 encoding an insect odorant receptor.
28. An isolated cDNA of claim 3 encoding a vertebrate odorant receptor.
29. An isolated cDNA of claim 3 encoding a fish odorant receptor.
30. An isolated cDNA of claim 3 encoding a mammalian odorant receptor.
31. An isolated cDNA of claim 30 wherein the mammalian odorant receptor is a human odorant receptor.
32. An isolated cDNA of claim 30 wherein the mammalian odorant receptor is a rat, dog or mouse odorant receptor.
33. An expression vector comprising the cDNA of claim 3 and the sequence elements necessary for replication and expression in a suitable host.
34. An expression vector comprising the cDNA of any of claims 4-19 and the sequence elements necessary for replication and expression in a suitable host.
35. A purified protein encoding an odorant receptor.

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36. A purified protein of claim 35 wherein the amino acid sequence is the sequence in Figure 9.
- 5 37. A purified protein of claim 35 wherein the amino acid sequence is the sequence in Figure 10.
38. A purified protein of claim 35 wherein the amino acid sequence is the sequence in Figure 11.
- 10 39. A purified protein of claim 35 wherein the amino acid sequence is the sequence in Figure 12.
40. A purified protein of claim 35 wherein the amino acid sequence is the sequence in Figure 13.
- 15 41. A purified protein of claim 35 wherein the amino acid sequence is the sequence in Figure 14.
42. A purified protein of claim 35 wherein the amino acid sequence is the sequence in Figure 15.
- 20 43. A purified protein of claim 35 wherein the amino acid sequence is the sequence in Figure 16.
- 25 44. A purified protein of claim 35 wherein the amino acid sequence is the sequence in Figure 17.
45. A purified protein of claim 35 wherein the amino acid sequence is the sequence in Figure 18.
- 30 46. A purified protein of claim 35 wherein the amino acid sequence is the sequence in Figure 19.
- 35 47. A purified protein of claim 35 wherein the amino acid sequence is the sequence in Figure 20.

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48. A purified protein of claim 35 wherein the amino acid sequence is the sequence in Figure 21.
- 5 49. A purified protein of claim 35 wherein the amino acid sequence is the sequence in Figure 22.
50. A purified protein of claim 35 wherein the amino acid sequence is the sequence in Figure 23.
- 10 51. A purified protein of claim 35 wherein the amino acid sequence is the sequence in Figure 24.
52. A purified protein of claim 35 wherein the amino acid sequence is the sequence in Figure 25.
- 15 53. A purified protein of claim 35 wherein the amino acid sequence is the sequence in Figure 26.
54. A purified protein of claim 35 wherein the amino acid sequence is the sequence in Figure 27.
- 20 55. A purified protein of claim 35 wherein the amino acid sequence is the sequence in Figure 28.
- 25 56. A purified protein of claim 35 wherein the amino acid sequence is the sequence in Figure 29.
57. A purified protein of claim 35 wherein the amino acid sequence is the sequence in Figure 31.
- 30 58. A purified protein of claim 35 encoding an insect odorant receptor.
59. A purified protein of claim 35 encoding a vertebrate odorant receptor.
- 35

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60. A purified protein of claim 35 encoding a fish odorant receptor.
- 5 61. A purified protein of claim 35 encoding a mammalian odorant receptor.
62. A purified protein of claim 61 wherein the mammalian odorant receptor is a human odorant receptor.
- 10 63. A purified protein of claim 61 wherein the mammalian odorant receptor is a rat, dog or mouse odorant receptor.
- 15 64. A purified protein of claim 35 which has 7 transmembrane regions and whose third cytoplasmic loop from the N-terminus is approximately 17 amino acid long.
- 20 65. A method of transforming cells which comprises transfecting a host cell with a suitable expression vector of claim 33.
- 25 66. A method of transforming cells which comprises transfecting a host cell with a suitable expression vector of claim 34.
67. Cells transformed by the method of claim 65.
- 30 68. Transformed cells of claim 67 wherein the cells are olfactory cells.
69. Transformed cells of claim 67 wherein the cells are non-olfactory cells.

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- 5 70. A method of identifying a desired odorant ligand comprising contacting transformed non-olfactory cells of claim 69, expressing a known odorant receptor with a series of odorant ligands and determining which ligands bind to the receptors present on the non-olfactory cells.
- 10 71. A method of identifying a desired odorant receptor comprising contacting a series of transformed non-olfactory cells of claim 69 with a known odorant ligand and determining which odorant receptor binds with the odorant ligand.
- 15 72. A method of detecting an odor which comprises:
- a) identifying a odorant receptor which binds the desired odorant ligand by the method of claim 71 and;
- 20 b) imbedding the receptor in a membrane such that when the odorant ligand binds with the receptor identified in a) above, a detectable signal is produced.
- 25 73. A method of claim 72 wherein the desired odorant is a pheromone.
- 30 74. A method of claim 72 wherein the desired odorant ligand is the vapors emanating from cocaine, marijuana, heroin, hashish, or angel dust.
- 35 75. A method of claim 72 wherein the desired odorant ligand is the vapors emanating from gasoline, natural gas or alcohol.

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76. A method of claim 72 wherein the desired odorant ligand is the vapors emanating from decayed human flesh.
- 5 77. A method of claim 72 wherein the desired odorant ligand is the vapors emanating from explosives, plastic explosives, firearms, or gun powder.
78. A method of claim 72 wherein the desired odorant ligand is toxic fumes, noxious fumes or dangerous fumes.
- 10 79. A method of claim 72 wherein the membrane is a cell membrane.
80. A method of claim 72 wherein the membrane is an olfactory cell membrane.
- 15 81. A method of claim 72 wherein the membrane is a synthetic membrane.
- 20 82. A method of claim 72 wherein the detectable signal is a color change, phosphorescence, or radioactivity.
83. A method of quantifying the amount of an odorant ligand present in a sample which comprises the method of claim 72 wherein the detectable signal is quantified.
- 25 84. A method of developing fragrances which comprises identifying a desired odorant receptor by the method of claim 71 then contacting non-olfactory cells, which have been transfected with an expression vector containing the cDNA of the desired odorant receptor such that the receptor is expressed upon the surface of the non-olfactory cell, with a series of compounds to determine which ones bind with the receptor.
- 30
- 35

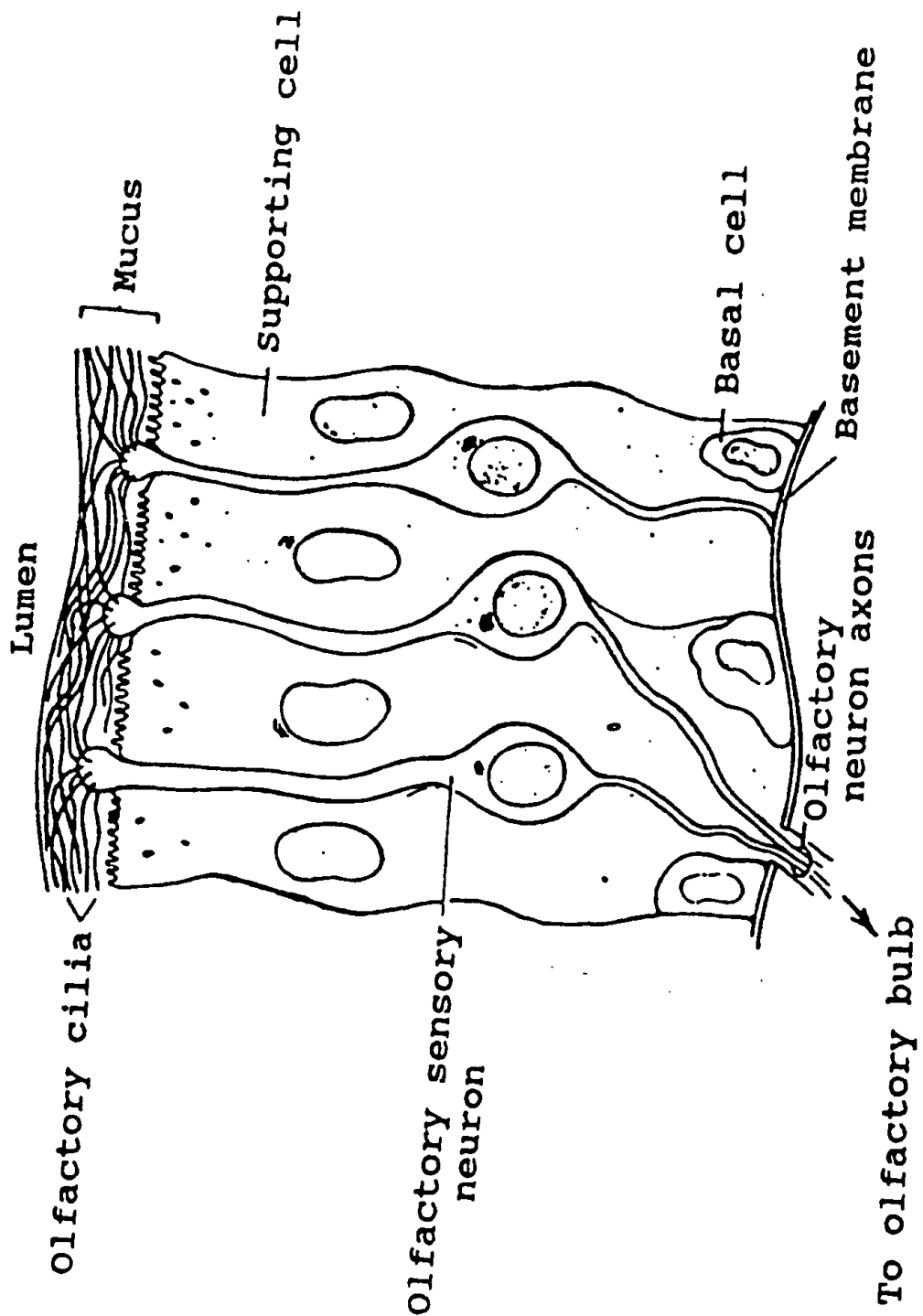
- 5 85. A method of identifying an odorant fingerprint which comprises contacting a series of cells, which have been transformed such that each express a known odorant receptor, with a desired sample and determining the type and quantity of the odorant ligands present in the sample.
- 10 86. A method of identifying odorant ligands which inhibit the activity of a desired odorant receptor which comprises contacting the desired odorant receptor with a series of compounds and determining which compounds inhibit the odorant ligand - odorant receptor interaction.
- 15 87. A method of identifying appetite suppressant compounds which comprises identifying odorant ligands by the method of claim 86 wherein the desired odorant receptor is that which is associated with the perception of food.
- 20 88. A method of controlling appetite in a subject which comprises contacting the olfactory epithelium of the subject with the odorant ligands identified by the method of claim 87.
- 25 89. A nasal spray, to control appetite comprising the compounds identified by the method of claim 87 in a suitable carrier.
- 30 90. A method of trapping odors which comprises contacting a membrane which contains multiples of the desired odorant receptor, with a sample such that the desired odorant ligand is absorbed by the binding of the odorant ligand to the odorant receptor.
- 35

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91. An odor trap employing the method of claim 90.
- 5 92. A method of controlling pest populations which comprises identifying odorant ligands by the method of claim 70 which are alarm odorant ligands and spraying the desired area with the identified odorant ligands.
- 10 93. A method of controlling a pest population which comprises identifying odorant ligands by the method of claim 70 which interfere with the interaction between the odorant ligands and the odorant receptors which are associated with fertility.
- 15 94. A method of claim 92 or 93 wherein the pest population is a population of insects.
95. A method of claim 92 or 93 wherein the pest population is a population of rodents.
- 20 96. A method of claim 95 wherein the population of rodents is a population of mice or rats.
- 25 97. A method of promoting fertility which comprises employing the method of claim 70 to identify odorant ligands which interact with the odorant receptors associated with fertility and administering the identified odorant ligands to a subject.
- 30 98. A method of inhibiting fertility which comprises employing the method of claim 70 to identifying odorant ligands which inhibit the interaction between the odorant ligands and the odorant receptors associated with fertility and administering the identified odorant ligands to a subject.

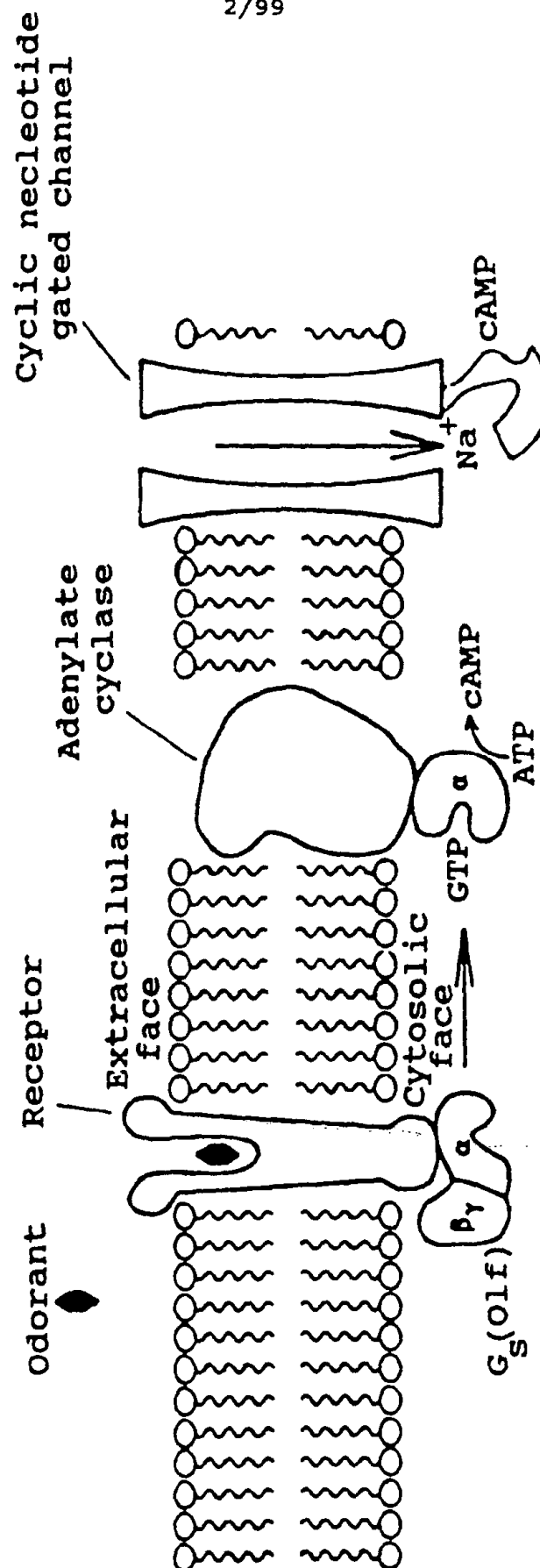
1/99

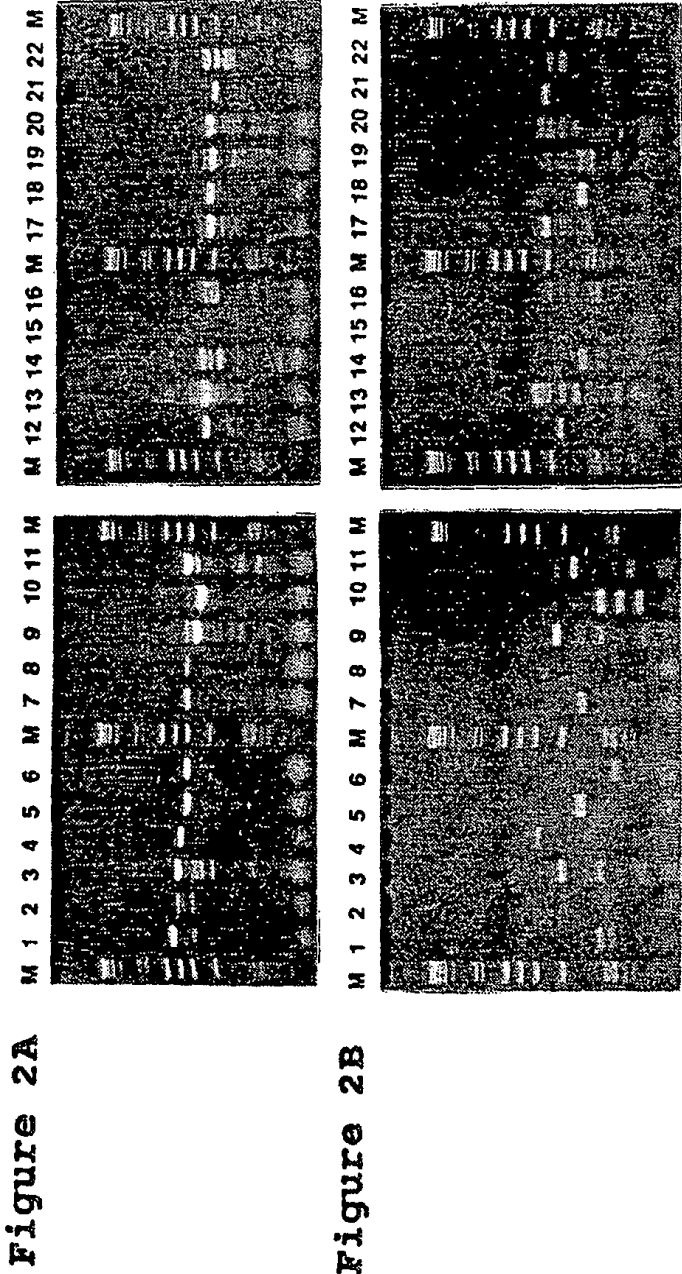
Figure 1A



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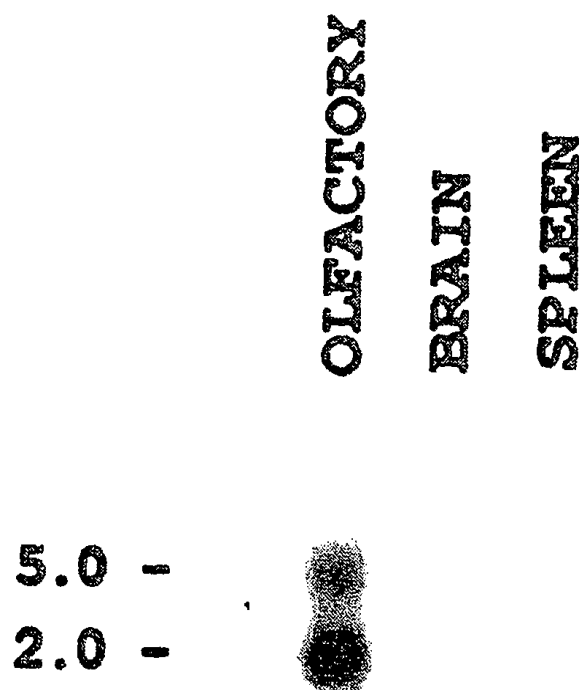
Figure 1B





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Figure 3



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Figur 4A

F3		M	D	S	S	N	R	T	R	V	S	E	11
F5		M	S	S	T	N	Q	S	S	V	T	E	11
F6	N A W	S	T	G	Q	N	L	S	T	P	G	P	14
F12		M	E	S	G	N	S	T	R	R	F	S	12
I3		M	N	-	-	N	Q	T	F	I	T	Q	9
I7		M	E	R	R	N	H	S	G	R	V	S	12
I8		M	N	-	-	N	K	T	V	I	T	H	9
I8		M	T	R	R	N	Q	T	A	I	S	Q	11
I14		M	T	G	N	N	Q	T	L	I	L	E	11
I15		M	T	E	E	N	Q	T	V	I	S	Q	11

F3	F	L	L	L	G	F	V	E	N	K	D	L	Q	P	25
F5	F	L	L	L	G	L	S	R	Q	P	Q	Q	Q	Q	25
F6	F	I	L	L	G	F	P	G	P	R	S	M	R	I	28
F12	F	F	L	L	G	F	T	E	N	P	Q	L	H	F	26
I3	F	L	L	L	G	L	P	I	P	E	E	H	Q	H	23
I7	F	V	L	L	G	F	P	A	P	A	P	L	R	V	26
I8	F	L	L	L	G	L	P	I	P	P	E	H	Q	Q	23
I9	F	F	L	L	G	L	P	F	P	P	E	Y	Q	H	25
I14	F	L	L	L	G	L	P	I	P	S	E	Y	H	L	25
I15	F	L	L	L	F	L	P	I	P	S	E	H	Q	H	25

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Figur 4B

	<u>I</u>	
F3	L I Y G L F L S M Y L V T V	39
F5	L L F L L F L I N Y L A T V	39
F6	G L F L L F L V M Y L L T V	42
F12	L I F A L F L S M Y L V T V	40
I3	L F Y A L F L V M Y L T T I	37
I7	L L F F L S L L X Y V L V L	40
I8	L F F A L F L I N Y L T T F	37
I9	L F Y A L F L A N Y L T T L	39
I14	L F Y A L F L A N Y L T I I	29
I15	V F Y A L F L S M Y L T T V	39

	<u>I</u>	
F3	I G N I S I I V A I I S D P	53
F5	L G N L L I I L A I G T D S	53
F6	V G N L A I I S L V G A H R	56
F12	L G N L L I I M A I I T Q S	54
I3	L G N L L I I V L V Q L D S	51
I7	T E N M L I I I A I R N H P	54
I8	L G N L L I V V L V Q L D S	51
I9	L G N L I I I I L I L L D S	53
I14	L G N L L I I V L V R L D S	53
I15	L G N L I I I I L I H L D S	53

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Figure 4C

	<u>II</u>														
F3	C	L	H	T	P	M	Y	F	F	L	S	N	L	S	67
F5	R	L	H	T	P	M	Y	F	F	L	S	N	L	S	67
F6	C	L	Q	T	P	M	Y	F	F	L	C	N	L	S	70
F12	H	L	H	T	P	M	Y	F	F	L	A	N	L	S	68
I3	Q	L	H	T	P	M	Y	L	F	L	S	N	L	S	65
I7	T	L	H	K	P	M	Y	F	F	L	A	N	M	S	68
I8	H	L	H	T	P	M	Y	L	F	L	S	N	L	S	65
I9	H	L	H	T	P	M	Y	L	F	L	S	N	L	S	67
I14	H	L	H	M	P	M	Y	L	F	L	S	N	L	S	67
I15	H	L	H	T	P	M	Y	L	F	L	S	N	L	S	67

	<u>II</u>														
F3	F	V	D	I	C	F	I	S	T	T	V	P	K	M	81
F5	F	V	D	V	C	F	S	S	T	T	V	P	K	V	81
F6	F	L	E	I	W	F	T	T	A	C	V	P	K	T	84
F12	F	V	D	I	C	F	T	S	T	T	I	P	K	M	82
I3	F	S	D	L	C	F	S	S	V	T	M	P	K	L	79
I7	F	L	E	I	W	Y	V	T	V	T	I	P	K	M	82
I8	F	S	D	L	C	F	S	S	V	T	M	L	K	L	79
I9	F	A	D	L	C	F	S	S	V	T	M	P	K	L	67
I14	F	S	D	L	C	F	S	S	V	T	M	P	K	L	67
I15	F	S	D	L	C	F	S	S	V	T	M	P	K	L	67

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Figur 4D

F3	L	-	-	-	-	V	N	I	Q	T	Q	N	N	V	91
F5	L	-	-	-	-	A	N	H	I	L	G	S	Q	A	91
F6	L	-	-	-	-	A	T	F	A	P	R	G	G	V	94
F12	L	-	-	-	-	V	N	I	Y	T	Q	S	K	S	92
I3	L	-	-	-	-	Q	N	M	R	S	Q	K	T	S	89
I7	L	A	G	F	I	G	S	K	E	N	H	G	Q	L	96
I8	L	-	-	-	-	Q	N	I	Q	S	Q	V	P	S	89
I9	L	-	-	-	-	Q	N	M	Q	S	Q	V	P	S	91
I14	L	-	-	-	-	Q	N	M	Q	S	Q	V	P	S	91
I15	L	-	-	-	-	Q	N	M	Q	S	Q	V	P	S	91

	<u>III</u>														
F3	I	T	Y	A	G	C	I	T	Q	I	Y	F	F	L	105
F5	I	S	F	S	G	C	L	T	Q	L	Y	F	L	A	105
F6	I	S	L	A	G	C	A	T	Q	M	Y	F	V	F	108
F12	I	T	Y	E	D	C	I	S	Q	M	C	V	F	L	106
I3	I	P	Y	G	G	C	L	A	Q	T	Y	F	F	M	103
I7	I	S	F	E	A	C	M	T	Q	L	Y	F	F	L	110
I8	I	S	Y	A	G	C	L	T	Q	I	F	F	F	L	103
I9	I	P	Y	A	G	C	L	A	Q	I	Y	F	F	L	105
I14	I	S	Y	T	G	C	L	T	Q	L	Y	F	F	M	105
I15	I	P	F	A	G	C	L	T	Q	L	Y	F	Y	L	105

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Figure 4E

	<u>III</u>	
F3	L F V E L D N F L L T I N A	119
F5	V F G N M D N F L L A V N S	119
F6	S L G C T E Y F L L A V N A	122
F12	V F A I L G N F L L A V N A	120
I3	V F G D M E S F L L V A N A	117
I7	G L G C T E C V L L A V N A	124
I8	L F G Y L G N F L L V A N A	117
I9	F F G D L G N F L L V A N A	119
I14	V F G D M E S F L L V V N A	119
I15	Y F A D L E S F L L V A N A	119

	<u>III</u>	
F3	Y D R Y V A I C H P M H Y T	133
F5	Y D R F V A I C H P L H Y T	133
F6	Y D R Y L A I C L P L R Y G	136
F12	Y D R Y V A X C H P L C Y T	134
I3	Y D R Y V A I C F P L H Y T	131
I7	Y D R Y V A I C H P L H Y P	138
I8	Y D R Y V A I C F P L H Y T	131
I9	Y D R Y V A I C F P L H Y M	133
I14	Y D R Y V A I C F P L R Y T	133
I15	Y D R Y V A I C F P L H Y M	133

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Figure 4F

	<u>IV</u>	
F3	V I N N Y K L C G F L V L V	147
F5	T K N T R Q L C V L L V V G	147
F6	G I N T P G L A M R L A L G	150
F12	V I V N H R L C I L L L L L	148
I3	S I N S P K L C T C L V L L	145
I7	V I V S S R L C V Q M A A G	152
I8	N I N S H K L C T C L L L V	145
I9	S I N S P K L C V S L V V L	147
I14	T I N S T K F C A S L V L L	147
I15	S I N S P K L C V S L V V L	147

	<u>IV</u>	
F3	S W I V S V L H A L F Q S L	161
F5	S W V V A N M N C L L H I L	161
F6	S W L C G F S A I T V P A T	164
F12	S W V I S I F H A F I Q S L	162
I3	L W M L T T S H A M M H T L	159
I7	S W A G G F G I S M V K V F	166
I8	F W I M T S S H A M M H T L	159
I9	S W V L T T F H A M L H T L	161
I14	L W M L T M T H A L L H T L	161
I15	S W V L T T F H A M L H T L	161

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Figur 4G

F3	M M L A L P F C T H L E I P	175
F5	L M A R K S F C A D N M I P	175
F6	L I A R L S F C G S R V I N	178
F12	I V L Q L T F C G D V K I P	176
I3	L A A R L S F C E N N V V L	173
I7	L I S R L S Y C G P N T I N	180
I8	L A A R L S F C E N N V L L	173
I9	L M A R L S F C E D S V I P	175
I14	L I A R L S F C E K N V I L	175
I15	L M A R L S F C A D N M I P	175

F3	H Y F C E P N Q V I Q L T C	189
F5	H F F C D G T P L L K L S C	189
F6	H F F C D I S P W I V L S C	192
F12	H F F C E L N Q L S Q L T C	190
I3	N F F C D L F V L L K L A C	187
I7	H F F C D V S P L L N L S C	194
I8	N F F C D L F V L L K L A C	187
I9	H Y F C D M S T L L K V A C	189
I14	H F F C D I S A L L K L S C	189
I15	H F F C D I S P L L K L S C	189

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Figur 4H

		V	
F3	S D A F L N D	L V I Y F T L	203
F5	S D T H L N E	L M I L T E G	203
F6	T D T Q V V E	L V S F G I A	206
F12	S D N F P S H	L I M N L V P	204
I3	S D T Y I N E	L M I F I M S	201
I7	T D M S T A E	L T D F V L A	208
I8	S D T Y V N E	L M I H I M G	201
I9	S D T H D N E	L A I F I L G	203
I14	S D I Y V N E	L M I Y I L G	203
I15	S D T H V N E	L V I F V M G	203

	V	
F3	V L L A T V P	L A G I F Y S 217
F5	A V V M V T P	F V C I L I S 217
F6	F C V I L G S	C G I T L V S 220
F12	V M L A A I S	F S G I L Y S 218
I3	T L L I I I P	F F L I V M S 215
I7	I F I L L G P	L S V T G A S 222
I8	V I I I V I P	F V L I V I S 215
I9	G P I V V L P	F L L I I V S 203
I14	G L I I I I P	F L L I V M S 203
I15	G L V I V I P	F V L I I V S 203

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Figure 4I

	<u>V</u>	
F3	Y F K I V S S I C A I S S V	231
F5	Y I H I T C A V L R V S S P	231
F6	Y A Y I I T T I I K I P S A	234
F12	Y F K I V S S I H S I S T V	232
I3	Y A R I I S S I L K V P S T	229
I7	Y M A I T G A V M R I P S A	236
I8	Y A K I I S S I L K V P S T	229
I9	Y A R I V S S I F K V P S S	231
I14	Y V R I F F S I L K F P S I	231
I15	Y A R V V A S I L K V P S V	231

	<u>VI</u>	
F3	H G K Y K A F S T C A S H L	245
F5	R G G W K S F S T C G S H L	245
F6	R G R H R A F S T C S S H L	248
F12	Q G K Y K A F S T C A S H L	246
I3	Q G I C K V F S T C G S H L	243
I7	A G R H K A F S T C A S H L	250
I8	Q S I H K V F S T C G S H L	243
I9	Q S I H K A F S T C G S H L	245
I14	Q D I Y K V F S T C G S H L	245
I15	R G I H K I F S T C G S H L	245

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Figure 4J

	<u>VI</u>	
F3	S V V S L F Y C T G L G V Y	259
F5	A V V C L F Y G T V I A V Y	259
F6	T V V L I W Y G S T I F L H	262
F12	S I V S L F Y S T G L G V Y	260
I3	S V V S L F Y G T I I G L Y	257
I7	T V V I I F Y A A S I F I Y	264
I8	S V V S L F Y G T I I G L Y	257
I9	S V V S L F Y G T V I G L Y	259
I14	S V V T L F Y G T I F G I Y	259
I15	S V V S L F Y G T I I G L Y	259

	<u>VI</u>	<u>VII</u>	
F3	L S S A A N N S S Q A S A T		273
F5	F N P S S S H L A G R D M A		273
F6	V R T S V E S S L D L T K A		276
F12	V S S A V V Q S S H S A A S		274
I3	L C P A G N N S T V K E M V		271
I7	A R P K A L S A F D T N K L		278
I8	L C P S G D N F S L K G S A		271
I9	L C P S A N N S T V K E T V		273
I14	L C P S G N N S T V K E I A		273
I15	L C P S A N N S T V K E T V		273

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Figur 4K

	<u>VII</u>	
F3	A S V M Y T V V T P M V N P	287
F5	A A V M Y A V V T P M L N P	287
F6	I T V L N T I V T P V L N P	290
F12	A S V M Y T V V T P M L N P	288
I3	M A M M Y T V V T P M L N P	285
I7	V S V L Y A V I V P L F N P	292
I8	M A M M Y T V V T P M L N P	285
I9	M S L M Y T M V T P M L N P	287
I14	M A M M Y T V V T P M L N P	287
I15	M A M M Y T V V T P M L N P	287

	<u>VII</u>	
F3	F I Y S L R N K D V K S V L	301
F5	F I Y S L R N S D M K A A L	301
F6	F I Y T L R N K D V K E A L	304
F12	F I Y S L R N K D V K R A L	302
I3	F I Y S L R N R D M K R A L	299
I7	I I Y C L R N Q D V K R A L	306
I8	F I Y S L R N R D M K Q A L	299
I9	F I Y S L R N R D I K D A L	301
I14	F I Y S L R N R D M K R A L	301
I15	F I Y S L R N R D M K E A L	301

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Figure 4L

F3	K K T L C E E V I R S P P S	315
F5	R K V L A M R F P S K Q -	313
F6	R R T V K G K -	311
F12	E R L L E G N C K V H H W T	316
I3	I R V I C S M K I T L -	310
I7	R R T L H L A Q D Q E A N T	320
I8	I R V T C S K K I S L P W -	312
I9	E K I M C K K Q I P S F L -	314
I14	I R V I C T K K I S L -	312
I15	I R V L C K K K I T F C L -	314

F3	L L H F F L V L C H L P C F	329
F5		
F6		
F12	G -	317
I3		
I7	N K G S K I G -	327
I8		
I9		
I14		
I15		

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Figur 4M

F3
F5
F6
F12
I3
I7
I8
I9
I14
I15

I F C Y -

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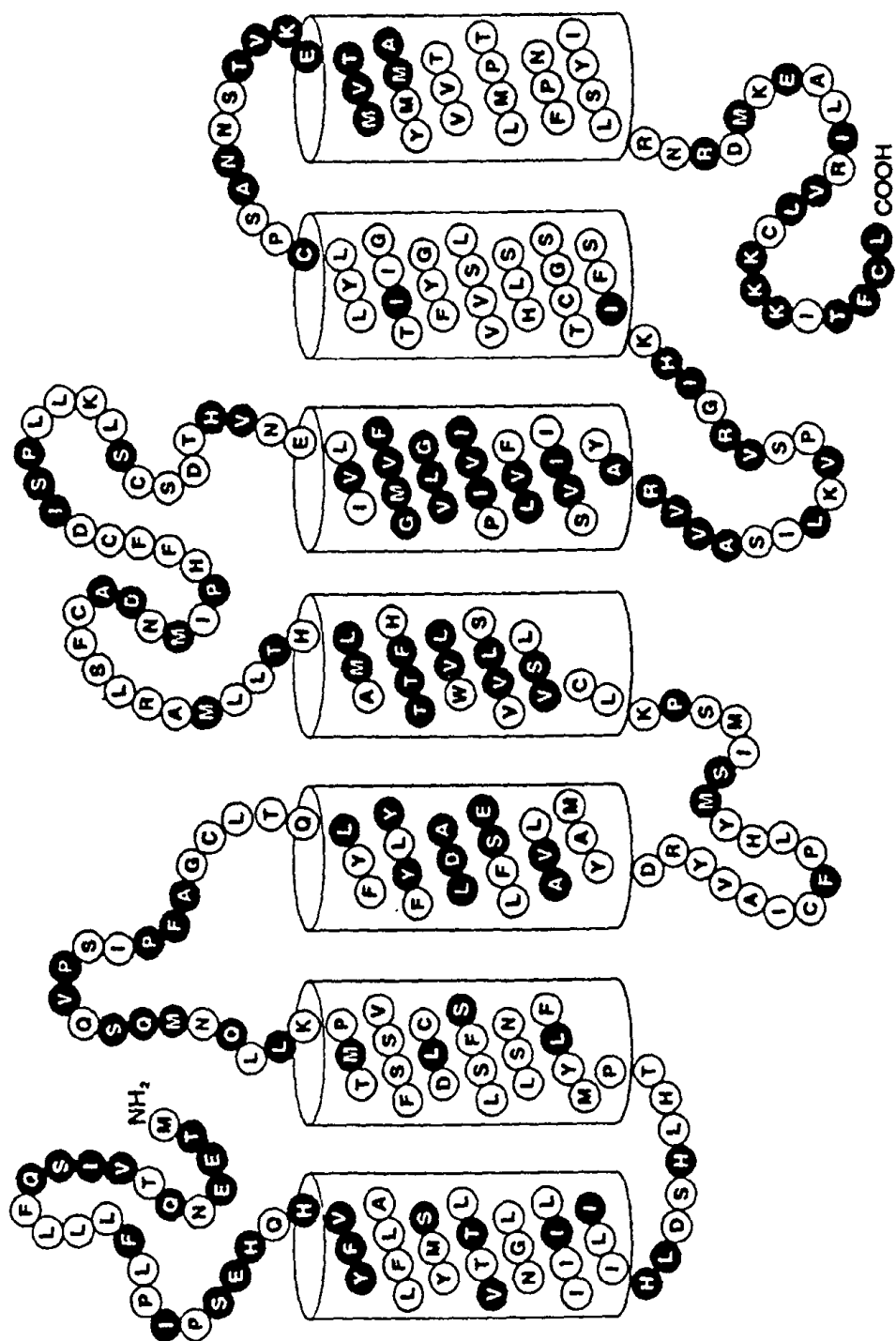


Figure 5

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Figure 6A(1)

	V													
F2	R	V	N	E	V	V	I	F	I	V	V	S	L	F
F3	F	L	N	D	L	V	I	Y	F	T	L	V	L	L
F5	H	L	N	E	L	M	I	L	T	E	G	A	V	V
F6	Q	V	V	E	L	V	S	F	G	I	A	F	C	V
F7	H	V	N	E	L	V	I	F	V	M	G	G	I	I
F8	F	P	S	H	L	T	M	H	L	V	P	V	I	L
F12	F	P	S	H	L	I	M	N	L	V	P	V	M	L
F13	F	P	S	H	L	I	M	N	L	V	P	V	M	L
F23	F	L	N	D	V	I	M	Y	F	A	L	V	L	L
F24	H	E	I	E	M	I	I	L	V	L	A	A	F	N
I3	Y	I	N	E	L	M	I	F	I	M	S	T	L	L
I7	S	T	A	E	L	T	D	F	V	L	A	I	F	I
I8	Y	V	N	E	L	M	I	H	I	M	G	V	I	I
I9	H	D	N	E	L	A	I	F	I	L	G	G	P	I
I11	H	L	N	E	L	M	I	L	T	E	G	A	V	V
I12	F	P	S	H	L	I	M	N	L	V	P	V	M	L
I14	Y	V	N	E	L	M	I	Y	I	L	G	G	L	I
I15	H	V	N	E	L	V	I	F	V	M	G	G	L	V

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Figure 6A(2)

	<u>V</u>
F2	L V L P F A L I I M S Y V R
F3	A T V P L A G I F Y S Y F K
F5	M V T P F V C I L I S Y I H
F6	I H G S C G I T L V S Y A Y
F7	L V I P F V L I I V S Y V R
F8	A A I S L S G I L Y S Y F K
F12	A A I S F S G I L Y S Y F K
F13	A A I S F S G I L Y S Y F K
F23	A V V P L L G I L Y S Y S K
F24	L I S S L L V V L V S Y L F
I3	I I I P F F L I V M S Y A R
I7	L L G P L S V T G A S Y M A
I8	I V I P F V L I V I S Y A K
I9	V V L P F L L I I V S Y A R
I11	M V T P F V C I L I S Y I H
I12	G A I S L S G I L Y S Y F K
I14	I I I P F L L I V M S Y V R
I15	I V I P F V L I I V S Y A R

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Figure 6A(3)

F2	I	V	S	S	I	L	K	V	P	S	S	Q	G	I
F3	I	V	S	S	I	C	A	I	S	S	V	H	G	K
F5	I	T	C	A	V	L	R	V	S	S	P	R	G	G
F6	I	I	T	T	I	I	K	I	P	S	A	R	G	R
F7	I	V	S	S	I	L	K	V	P	S	A	R	G	I
F8	I	V	S	S	I	R	S	M	S	S	V	Q	G	K
F12	I	V	S	S	I	H	S	I	S	T	V	Q	G	K
F13	I	V	S	S	I	R	S	V	S	S	V	K	G	K
F23	I	V	S	S	I	R	A	I	S	T	V	Q	G	K
F24	I	L	I	A	I	L	R	M	N	S	A	E	G	R
I3	I	I	S	S	I	L	K	V	P	S	T	Q	G	I
I7	I	T	G	A	V	M	R	I	P	S	A	A	G	R
I8	I	I	S	S	I	L	K	V	P	S	T	Q	S	I
I9	I	V	S	S	I	F	K	V	P	S	S	Q	S	I
I11	I	T	W	A	V	L	R	V	S	S	P	R	G	G
I12	I	V	S	S	V	R	S	I	S	S	V	Q	G	K
I14	I	F	F	S	I	L	K	F	P	S	I	Z	D	I
I15	V	V	A	S	I	L	K	V	P	S	V	R	G	I

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Figure 6A(4)

F2	Y	K
F3	Y	K
F5	W	K
F6	H	R
F7	R	K
F8	Y	K
F12	Y	K
F13	Y	K
F23	Y	K
F24	R	K
I3	C	K
I7	H	K
I8	H	K
I9	H	K
I11	W	K
I12	H	K
I14	Y	K
I15	H	K

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Figure 6B

	V													
F12	F	P	S	H	L	I	M	N	L	V	P	V	M	L
F13	F	P	S	H	L	I	M	N	L	V	P	V	M	L
F8	F	P	S	H	L	T	M	H	L	V	P	V	I	L
I12	F	P	S	H	L	I	M	N	L	V	P	V	M	L
F23	F	L	N	D	V	I	M	Y	F	A	L	V	L	L
F3	F	L	N	D	L	V	I	Y	F	T	L	V	L	L

	V													
F12	A	A	I	S	F	S	G	I	L	Y	S	Y	F	K
F13	A	A	I	S	F	S	G	I	L	Y	S	Y	F	K
F8	A	A	I	S	L	S	G	I	L	Y	S	Y	F	K
I12	G	A	I	S	L	S	G	I	L	Y	S	Y	F	K
F23	A	V	V	P	L	L	G	I	L	Y	S	Y	S	K
F3	A	T	V	P	L	A	G	I	F	Y	S	Y	F	K

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Figure 6B (Continued)

F12	I	V	S	S	I	H	S	I	S	T	V	Q	G	K
F13	I	V	S	S	I	R	S	V	S	S	V	K	G	K
F8	I	V	S	S	I	R	S	M	S	S	V	Q	G	K
I12	I	V	S	S	V	R	S	I	S	S	V	Q	G	K
F23	I	V	S	S	I	R	A	I	S	T	V	Q	G	K
F3	I	V	S	S	I	C	A	I	S	S	S	H	G	K

F12	Y	K
F13	Y	K
F8	Y	K
I12	H	K
F23	Y	K
F3	Y	K

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Figure 6C

					<u>V</u>								
F7	H	V	N	E	L	V	I	F	V	M	G	G	I
I15	H	V	N	E	L	V	I	F	V	M	G	G	L
I3	Y	I	N	E	L	M	I	F	I	M	S	T	L
I8	Y	V	N	E	L	M	I	H	I	M	G	V	I
I9	H	D	N	E	L	A	I	F	I	L	G	G	P
I14	Y	V	N	E	L	M	I	Y	I	L	G	G	L

					<u>V</u>								
F7	L	V	I	P	F	V	L	I	I	V	S	Y	V
I15	I	V	I	P	F	V	L	I	I	V	S	Y	A
I3	I	I	I	P	F	F	L	I	V	M	S	Y	A
I8	I	V	I	P	F	V	L	I	V	I	S	Y	A
I9	V	V	L	P	F	L	L	I	I	V	S	Y	A
I14	I	I	I	P	F	L	L	I	V	M	S	Y	V

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Figure 6C (Continued)

F7	I	V	S	S	I	L	K	V	P	S	A	R	G	I
I15	V	V	A	S	I	L	K	V	P	S	V	R	G	I
I3	I	I	S	S	I	L	K	V	P	S	T	Q	G	I
I8	I	I	S	S	I	L	K	V	P	S	T	Q	S	I
I9	I	V	S	S	I	F	K	V	P	S	S	Q	S	I
I14	I	F	F	S	I	L	K	F	P	S	I	Q	D	I

F7	R	K
I15	H	K
I3	C	K
I8	H	K
I9	H	K
I14	Y	K

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Figure 6D

[illegible]

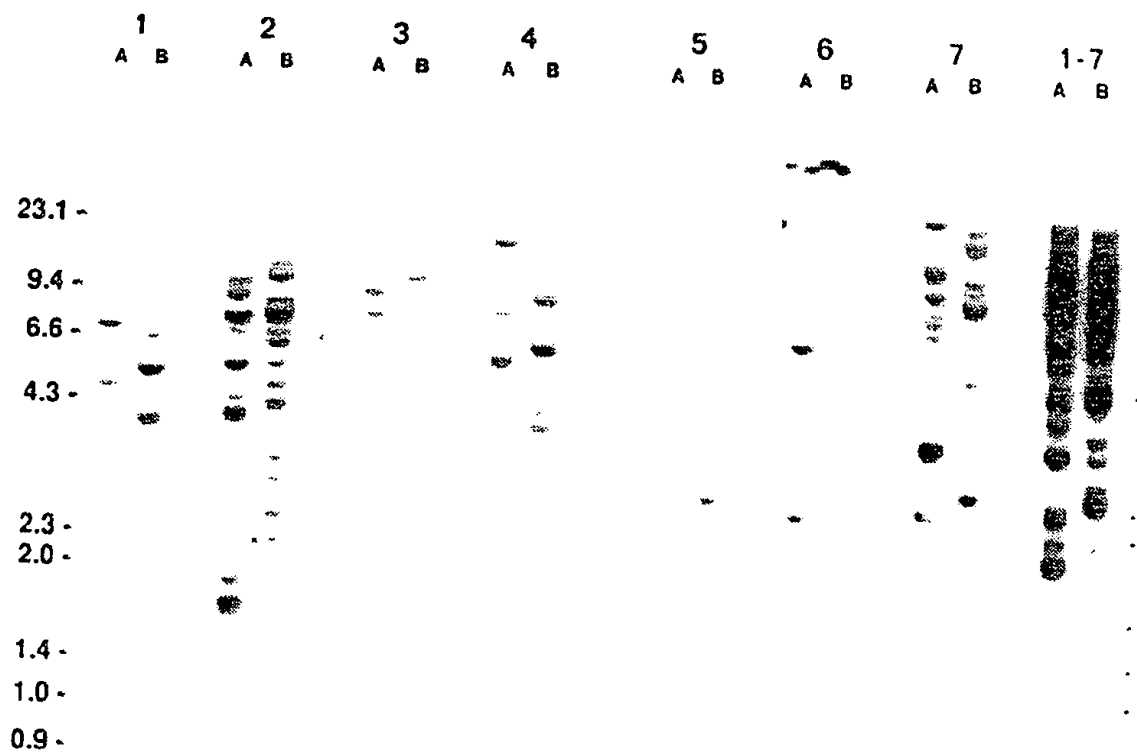
	V												
F5	N	V	T	P	F	V	C	I	L	S	Y	I	H
I11	N	V	T	P	F	V	C	I	L	S	Y	I	H

F5 I T C A V L R V S S P R G G
I11 I T W A V L R V S S P R G G

F5 W K
I11 W K

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Figure 7



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Figure 8

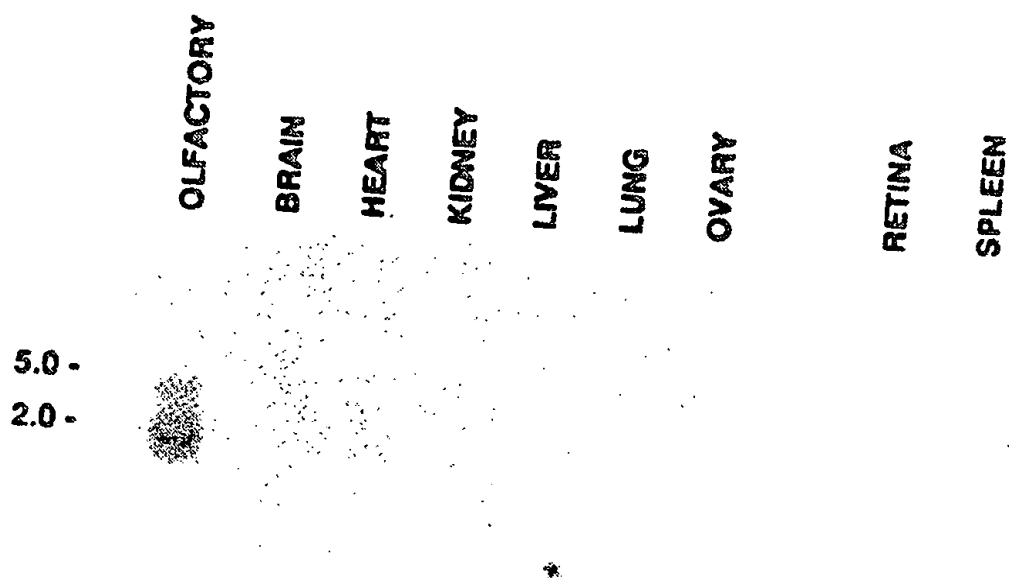


Figure 9A Translated sequence of F3T.D1S

10 * 20 * 30 * 40 * 50 * 60 *
 ATG GAC TCA AGC AAC AGG ACA AGA GTT TCA GAA TTT CTT CTT GGA TTT GTA GAA AAC
 M D S S N R T R V S S E F L L L C F V E N

70 * 80 * 90 * 100 * 110 * 120 *
 AAA GAC CTA CAA CCC CTT ATT TAT GGT CTT TTT CTC TCT ATG TAC CTG GTT ACT GTC ATT
 K D L Q P L I Y G L F L S M Y L V T V I

130 * 140 * 150 * 160 * 170 * 180 *
 GGA AAC ATA TCC ATT ATT GTG GCT ATC ATT TCA GAT CCC TGT CTG CAG ACC CCC ATG TAT
 G N I S I I V A I I S D P C L H T P M Y

190 * 200 * 210 * 220 * 230 * 240 *
 TTC TTC CTC TCT AAC CTG TCC TTT GTG GAC ATC TGT TTC ATT TCA ACC ACT GTT CCA AAC
 F F L S N L S F V D I C F I S T T V P K

250 * 260 * 270 * 280 * 290 * 300 *
 ATG TTA GTG AAC ATC CAG ACC CAA AAC AAT GTC ATC ACC TAT GCA GGA TGC ATT ACC CAG
 M L V N I Q T Q N N V I T Y A G C I T Q

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Figure 9B

310	320	330	340	350	360
* ATA TAC TTT TTC TTG CTC TTT GTA GAA TTG GAC AAC TTC TTG CTG ACT ATC ATG GCC TAT I Y F F L L L F V E L L D N F L L T I M A Y	* 320	* 330	* 340	* 350	* 360
370	380	390	400	410	420
* GAC CGT TAC GTA GCC ATC TGT CAC CCG ATG CAC TAC ACA GTT ATC ATG AAC TAC AAG CTC D R Y V A I C H P M H Y T V I M N Y K L	* 380	* 390	* 400	* 410	* 420
430	440	450	460	470	480
* TGT GGA TTT CTG GTT CTG GTA TCT TGG ATT GTA AGT GTT CTG CAT GCC TTG TTT CAA AGC C G F L L V L V S W I V S V L H A L F Q S	* 440	* 450	* 460	* 470	* 480
490	500	510	520	530	540
* TTG ATG ATG TTG GCG CTG CCC TTC TGC ACA CAT CTG GAA ATC CCA CAC TAC TTC TGT GAA L M M L L A L P F C T H L L E I P H Y F C E	* 500	* 510	* 520	* 530	* 540
550	560	570	580	590	600
* CCT AAT CAG GTG ATT CAA CTC ACC TGT TCT GAT GCA TTT CTT AAT GAT CTT GTG ATA TAT P N Q V I Q L L T C S D A F L N D L V I Y	* 560	* 570	* 580	* 590	* 600
610	620	630	640	650	660

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Figure 9C

[illegible]

33/99

Figure 9D

CTG AAA	910	CTT TGT	920	ATA AGC	930	TCC CTA	940	CTT CAT	950	TTC TTC	960
L K	*	L C	*	I R	*	S L	*	L H	*	F F	*
K T		E E		S S		P S		P P		F F	
AAA ACT		GAG GAA		AGT AGT		CCA CCT		CCA CCT		TTC TTC	
L K		L C		I R		P S		P P		F F	
T T		E E		S S		P S		P P		F F	
CTG AAA		GAG GAA		AGT AGT		CCA CCT		CCA CCT		TTC TTC	
L K		L C		I R		P S		P P		F F	
T T		E E		S S		P S		P P		F F	
CTG AAA		GAG GAA		AGT AGT		CCA CCT		CCA CCT		TTC TTC	
L K		L C		I R		P S		P P		F F	
T T		E E		S S		P S		P P		F F	

CTA GTG	970	CTC CCT	980	ATT TTT	990	TGT TAT	1000
L V	*	L P	*	I F	*	C Y	*
L C		L P		I F		C Y	
T T		C C		TTT TTT		TGT TAT	
CTA GTG		CTC CCT		ATT TTT		TGT TAT	
L V		L P		I F		C Y	
L C		L P		I F		C Y	
T T		C C		TTT TTT		TGT TAT	

Translation begun with base no. 57

Translated to base no.1058

Sequence printed from base no. 57 to base no.1058

Sequence numbered beginning with base no. 57

Figure 10A Translated sequence of F5T.D1S

10	20	30	40	50	60
* ATG AGC AGC ACC AAC CAG TCC AGT GTC ACC GAG TTC CTC CTC CTG GGA CTC TCC AGG CAG	* M S S T N Q CAG TCC S S S V T E F L L L L G L S R Q	* 70	* 80	* 90	* 100
* CCC CAG CAG CAG CTC CTC TTC CTC TTC CTC ATC ATG TAC CTG CCC ACT GTC CTG	* P Q Q Q Q L L L F L L F L I M Y L A T V L	* 130	* 140	* 150	* 160
* GGA AAC CTG CTC ATC CTC GCT ATT GGC ACA GAC TCC CGC CTG CAC ACC CCC ATG TAC	* G N L L I I L A I G T D S R L H T P M Y	* 190	* 200	* 210	* 220
* TTC TTC CTC AGT AAC CTG TCC TTT CTG GAT GTC TGC TCC TTC TCC TCT ACC ACT GTC CCT AAA	* F F L S N L L S F V D V C F S S S T T V P K	* 250	* 260	* 270	* 280
* GTT CTG GCC AAC CAT ATA CTT GGG AGT CAG GCC ATT TCC TTC TCT GGG TGT CTC ACC CAG	* V L A N H I L G S Q A I S F S G C L T Q				

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Figure 10B

CTG TAT TTT CTC GCT GTG TTT GGT AAC ATG GAC AAT TTC CTG GCT CTG ATG TCC TAT	310	320	330	340	350	360
L Y F L A V F G N M D N F L L A V M S Y	*	*	*	*	*	*
GAC CGA TTT GTG GCC ATA TGC CAC CCT TTA CAC TAC ACA AAG ATG ACC CGT CAG CTC	370	380	390	400	410	420
D R F V A I C H P L L H Y T T K M T R Q L	*	*	*	*	*	*
IGT GTC CTG CTT GTT GTG GGG TCA TGG GTT GTA GCC AAC ATG AAT TGT CTG TTG CAC ATA	430	440	450	460	470	480
C V L L V V G G S S W V V V A N M N C L L H I	*	*	*	*	*	*
CTG CTC ATG GCT CGA CTC TCC TCC TTC TGT GCA GAC AAC ATG ATC CCC CAC TTC TTC TGT GAT	490	500	510	520	530	540
L L M A R L S F C A D N M I P H F C D	*	*	*	*	*	*
GGA ACT CCC CTC CTG AAA CTC TCC TCC TCA GAC ACA CAT CTC AAT GAG CTG ATG ATT CTT	550	560	570	580	590	600
G T P L L K L S C S D T H L L N E L M I L	*	*	*	*	*	*
	610	620	630	640	650	660

Figure 10C

ACA	GAG	GGA	GCT	CTG	CTG	ATG	GTC	ACC	CCA	TTT	GTC	TGC	ATC	CTC	ATC	TCC	TAC	ATC	CAC	*
T	E	G	A	V	V	M	V	T	P	F	V	C	I	L	I	S	Y	I	H	*
670					680				690			700				710			720	
ATC	ACC	TGT	GCT	CTG	CTC	AGA	GTC	TCA	TCC	CCC	AGG	GGA	GGA	TGG	AAA	TCC	TTC	TCC	ACC	*
I	T	C	A	V	L	R	V	S	S	P	R	G	G	W	K	S	F	S	T	*
730					740				750			760				770			780	
TGT	GGC	TCC	CAC	CTG	GCT	GTC	GTC	TGC	CTC	TTC	TAT	GGC	ACC	GTC	ATC	GCT	GTG	TAT	TTC	*
C	G	S	H	L	A	V	V	C	L	F	Y	G	T	V	I	A	V	Y	F	*
790					800				810			820				830			840	
AAC	CCA	TCA	TCC	TCT	CAC	TTA	GCT	GGG	AGG	GAC	ATG	GCA	GCT	GCA	GTG	ATG	TAT	GCA	GTG	*
PRONUC/TRA OPTION																				
N	P	S	S	S	H	L	A	G	R	D	M	A	A	A	V	M	Y	A	V	

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Figure 10D

850	860	870	880	890	900
* GTG ACC CCA ATG CTG AAC CCT TTC ATC TAT AGC CTG AGG AAC AGC AGC GAC ATG AAA CCA GCT	* 860	* 870	* 880	* 890	* 900
V T P M L N P F I Y S L R N S D M K A A					
910	920	930	940		
* TTA AGG AAA GTG CTC GCC ATG AGA TTT CGA TCT AAG CAG TAA	* 920	* 930	* 940		
L R K V L A M R F P S K Q -					

Translation begun with base no. 62

Translated to base no.1003

Sequence printed from base no. 62 to base no.1003

Sequence numbered beginning with base no. 62

Figure 11A Translated sequence of F6T.D1s

10 * 20 * 30 * 40 * 50 * 60 *
 ATG GCT TGG AGT ACT GGC CAG AAC CTG TCC ACA CCA GGA CCA TTC ATC TTG CTG GGC TTC
 M A W S T I G Q N L S T P G P F I L L C G F

70 * 80 * 90 * 100 * 110 * 120 *
 CCA GGG CCA AGG AGC ATG CGC ATT GGG CTC TTC CTG CTT TTC CTG CTC ATG TAT CTG CTT
 P G P R S M R I G L F L L F L V M Y L L

130 * 140 * 150 * 160 * 170 * 180 *
 ACC GTA CTT GGA AAC CTA GCC ATC ATC ATC TCC CTG GTA GGT GCC CAC AGA TGC CTA CAG ACA
 T V V G G N L A I I S L V G A H R C L Q T

190 * 200 * 210 * 220 * 230 * 240 *
 CCC ATG TAC TTC TTC CTC TGC AAC CTC TCC TTC CTG GAG ATC TGG TTC ACC ACA GCC TGC
 P M Y F F L C N L S F L E I W F T A C

250 * 260 * 270 * 280 * 290 * 300 *
 GTA CCC AAG ACC CTG GCC ACA TTT GCG CCT CGG GGT GGA GTC ATT TCC TTG GCT GGC TGT
 V P K T L A T F A P R G G V I S L A G C

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Figure 11B

310 * 320 * 330 * 340 * 350 * 360 *
 GCC ACA CAG ATG TAC TTT GTC TTT TCT TTG GGC TGT ACC GAG TAC TTC CTG CTG GCT GTG
 A T Q M Y F V F S L G C T E Y F L L A V

370 * 380 * 390 * 400 * 410 * 420 *
 ATG GCT TAT GAC CGC TAC CTG GGC ATC TGC CTG CCA CTG CGC TAT GGT GGC ATC ATG ACT
 M A Y D R Y L A I C L P L R Y G G I M T

430 * 440 * 450 * 460 * 470 * 480 *
 CCT GGG CTG GCG ATG CGG TTG GGC CTG GGA TCC TGG CTG TGT TGT GGG TTT TCT GCA ATC ACA
 P G L A M R L L A L G S W L C G F S A I T

490 * 500 * 510 * 520 * 530 * 540 *
 GTT CCT GCT ACC CTC ATT GCC CGC CTC TCT TTC TGT GGC TCA CGT GTC ATC AAC CAC TTC
 V P A T L I A R L S F C G S R V I N H F

550 * 560 * 570 * 580 * 590 * 600 *
 TTC TGT GAC ATT TCG CCC TGG ATA GTG CTT TCC TGC ACC GAC ACG CAG CTG GTG GAA CTG
 F C D I S P W I V L S C T D T Q V V E L

610 620 630 640 650 660

Figure 11c

* GCG	* TTC	* TGT	* GGT	* ATC	* ACA	* CTA	* GTC	* TCC
TCC TTT GGC ATT GCC TTC TGT GTT ATT CTG GGC TCG TCG TGT GGT ATC ACA CTA CTC TTC	V S F G I A F C V I L G C S C G I T L V S							
670	680	690	700	710	720			
* TAT	* GCT	* TAC	* ATC	* ACC	* ACT	* ATC	* ATC	* GCC
Y A Y I I T T I I I K I P S A R G C GGC CGC CAG CGC GCC								
730	740	750	760	770	780			
* TTC	* TCA	* ACC	* TGC	* TCA	* TCC	* CAT	* CTC	* ACT
F S T C S S H L T V V V L I W Y G S T I F								
790	800	810	820	830	840			
* TTG	* CAT	* GTG	* AGG	* ACC	* TCG	* GTA	* GAG	* AGC
PRONUC/TRA OPTION								
L H V R T S V E S S S L D L T K A I T V L								

41/99

Figure 11D

850	*	AAC ACC ATT GTC ACA CCT GTG CTG AAC CCT TTC ATA TAT ACT CTG AGG AAC AAG GAT CTC	880	*	890	*	900	*
		N T I V T P P V L N P F I Y T L R N K D V						
910	*	AAG GAA CCT CTG CGC AGG ACC GTG AAG GCG AAG TGA	920	*	930	*		
		K E A L R R T V K G K -						

Translation begun with base no. 75
 Translated to base no.1010
 Sequence printed from base no. 75 to base no.1010
 Sequence numbered beginning with base no. 75

Figure 12A Translated sequence of F12T.D1S

10	20	30	40	50	60
* ATG GAA TCA GGG AAC AGC ACA AGA AGA TTT TCA AGT TTT TTT CTT CTT GGA TTT ACA GAA	* M E S C N S T R R F F S F F L L G F T E	* 30	* 40	* 50	* 60
70	80	90	100	110	120
* AAC CCA CAA CTT CAC TTC CTC ATT TTT GCA CTA TTC CTG TCC ATG TAC CTG GTA ACA CTG	* N P Q L H C F L I F A L F L S M Y L V T V	* 90	* 100	* 110	* 120
130	140	150	160	170	180
* CTT GGG AAC CTG CTT ATC ATT ATG GCC ATC ATC ACA CAG TCT CAT TTG CAT ACA CCC ATG	* L G N L L I I M A I I T Q S H L H T P M	* 150	* 160	* 170	* 180
190	200	210	220	230	240
* TAC TTT TTC CTT GCT AAC CTA TCC TTT GTG GAC ATC TGT TTC ACC TCC ACC ACC ATC CCA	* Y F F L A N L S F V D I C F T S T T I P	* 210	* 220	* 230	* 240
250	260	270	280	290	300
* TAC TTT TTC CTT GCT AAC CTA TCC TTT GTG GAC ATC TGT TTC ACC TCC ACC ACC ATC CCA	* Y F F L A N L S F V D I C F T S T T I P	* 270	* 280	* 290	* 300

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Figure 12B

AAG ATG TTG GTA AAT ATA TAC ACC CAG AGC AAG AGC ATC ACC TAT GAA GAC TGT ATT AGC
 K M L V N I Y T Q S K S I T Y E D C I S
 310 * 320 * 330 * 340 * 350 * 360 *
 CAG ATG TGT CTC TTC TTG GTT TTC GCA GAA TTG GGC AAC TTT CTC CTG GCT GTG ATG GCC
 Q M C V F L V F A E L G N F L L A V M A
 370 * 380 * 390 * 400 * 410 * 420 *
 TAT GAC CGA TAT GTG GCT A-C TGT CAC CCA CTG TGT TAC ACA GTC ATT GTG AAC CAC CCG
 Y D R Y V A X C C H P L C Y T V I V N H R
 430 * 440 * 450 * 460 * 470 * 480 *
 CTC TGT ATC CTG CTG CTT CTG CTG TCG TCG GTT ATC AGC ATT TTC CAT GCG TTC ATA CAG
 L C I L L L L L S S W V I S I F H A F I Q
 490 * 500 * 510 * 520 * 530 * 540 *
 ACC TTA ATT GTG CTA CAG TTG ACC TTC TGT TGT GGA GAT GTG AAA ATC CCT CAC TTC TTC TGT
 S L I V L Q L L T F C C G D V K I P H F F C
 550 * 560 * 570 * 580 * 590 * 600 *
 GAA CTT AAT CAG CTG TCC CAA CTC ACC TGT TGT TCA GAC AAC TTT CCA AGT CAC CTC ATA ATG
 E L N Q L L S Q L T C S D N F P S H L I M

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Figure 12D

850	860	870	880	890	900
* GTG CTC ACC CCC ATG CTG AAC CCC TTC ATT TAT AGT CTA AGG AAT AAA CAT GTG AAG AGA	* V T P M L N P F I Y S L R N K D V K R				
910	920	930	940	950	
* GCT CTG GAA AGA CTG TTA GAA GGA AAC TGT AAA GTG CAT TGG ACT GGA TGA	* A L E R L L E G N C K V H H T C -				

Translation begun with base no. 173

Translated to base no.1126

Sequence printed from base no. 173 to base no.1126

Sequence numbered beginning with base no. 173

Figure 13A Translated sequence of I3T.D1S

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10	20	30	40	50	60
* ATG AAC AAT CAA ACT TTC ATC ACC CAA TTC CTT CTC CTG GGA CTG CCC ATC CCT GAA GAA M N N Q T F I T Q Q F L L L G L P I P E E	* 70	* 80	* 90	* 100	* 110
* CAT CAG CAC CTG TTC TAT GCG TTG TTC CTG GTC ATG TAC CTC ACC ACC ATC TTG GGA AAC H Q H L F Y A L F L V M Y L T T I L G N	* 120	* 130	* 140	* 150	* 160
* TTG CTA ATC ATT GTA CTT GTT CAA CTG GAC TCC CAG CTC CAC ACA CCT ATG TAT TTG TTT L L I I V L V Q L D S Q L H T P M Y L F	* 170	* 180	* 190	* 200	* 210
* CTC AGC AAT TTG TCT TTC TCT GAT CTA TGT TTT TCC TCT GTC ACA ATG CCC AAG CTG CTG L S N L S F S D L C F S S V T M P K L L	* 220	* 230	* 240	* 250	* 260
* CAG AAC ATG AGG AGC CAG GAC ACA TCC ATT CCC TAT GGA GGC TGC CTG GCA CAA ACA TAC Q N M R S Q D T S I P Y G G C L A Q T Y	* 270	* 280	* 290	* 300	* 310

47/99

Figure 13B

310	320	330	340	350	360
* TTC TTT ATG GTT TTT GGA GAT ATG GAG AGT TTC CTT CTT GTG GCC ATG GCC TAT GAC CGC	* F F M V F F G D M E S F L L V A M A Y D R	* 370	* 380	* 390	* 400
* TAT GTG GCC ATO TGC TTC CCT CTG CAT TAC ACC AGC ATC ATG AGC CCC AAG CTC TGT ACT	* Y V A I C F P L H Y T S I M S P K L C T	* 410	* 420	* 430	* 440
* TGT CTA GTG CTG TTA TTG TGG ATG CTG ACC ACA TCC CAT GCC ATG ATG CAC ACA CTG CTT	* C L V L L L L W M L T T S H A M M H T L L	* 450	* 460	* 470	* 480
* GCA GCA AGA TTG TCT TTT TGT GAG AAC AAT GTG CTC CTC ATG TTC TTC TGT GAC CTA TTT	* A A R L L S F F C E N N V V L N F F C D L F	* 490	* 500	* 510	* 520
* GTT CTC CTA AAG CTG GCC TGC TCA GAC ACT TAT AAT GAG TTG ATG ATA TTT ATC ATG	* V L L K L L A C S D T Y I N E L M I F I M	* 530	* 540	* 550	* 560
* 610	* 620	* 630	* 640	* 650	* 660

Figure 14A Translated sequence of I7T.D1S

10 * 20 * 30 * 40 * 50 * 60 *
 ATG GAG CGA AGG AAC CAC AGT GGG AGA GTG AGT GAA TTT GTG TTG CTG GGT TTC CCA CCT
 M E R R N H S C R V S E F V L L G G F P A

 70 * 80 * 90 * 100 * 110 * 120 *
 CCT GCC CCA CTG CGA GTA CTA CTA TTT TTC CTT TCT CTT CTG G-C TAT GTG TTG GTG TTG
 P A P L R V L L L F F L S L L L X Y V L V L

 130 * 140 * 150 * 160 * 170 * 180 *
 ACT GAA AAC ATG CTC ATC ATT ATA GCA ATT AGG AAC CAC CCA ACC CTC CAC AAA CCC ATG
 T E N M L I I I A I R N H P T L H K P M

 190 * 200 * 210 * 220 * 230 * 240 *
 TAT TTT TTC TTG GCT AAT ATG TCA TTT CTG GAG ATT TGG TAT GTG ACT GTT ACG ATT CCT
 Y F F L A N M S F L L E I W Y V T V T I P

 250 * 260 * 270 * 280 * 290 * 300 *
 AAG ATG CTC GCT GGC TTC ATT GGT TCC AAG GAG AAC CAT GGA CAG CTG ATC TCC TTT GAG
 K M L A G F I G S K E N H G Q L I S F E

Figure 14B

GCA TGC ATG ACA CAA CTC TAC TTT TTC CTC GGC TTG GGT TGC ACA GAG TGT GTC CTT CTT	310	320	330	340	350	360
A C M T Q L Y F F L G L G C T E C V L	*	*	*	*	*	*
GCT GTG ATG GCC TAT GAC CGC TAT GTG GCT ATC TGT CAT CCA CTC CAC TAC CCC GTC ATT	370	380	390	400	410	420
A V M A Y D R Y V A I C H P L H Y P V I	*	*	*	*	*	*
GTC AGT AGC CGG CTA TGT GTG CAG ATG GCA GCT GGA TCC TGG GCT GGA GGT TTT GGT ATC	430	440	450	460	470	480
V S S R L C V Q M A A G S W A G G F G I	*	*	*	*	*	*
TCC ATG GTT AAA GTT TTC CTT ATT TCT CGC CTG TCT TAC TGT TGT GGC CCC AAC ACC ATC AAC	490	500	510	520	530	540
S M V K V F L I S R L S Y C G P N T I N	*	*	*	*	*	*
CAC TTT TTC TGT GAT GTG TCT CCA TTG CTC AAC CTG TCA TGC ACT GAC ATG TCC ACA GCA	550	560	570	580	590	600
H F F C D V S P L L N L S C T D M S T A	*	*	*	*	*	*

50/99

51/99

Figure 14C

610	*	620	*	630	*	640	*	650	*	660	*
GAG CTT ACA GAC TTT GTC CTG GGC ATT TTT ATT CTG CTG GGA CCG CTC TCT GTC ACT GCG											
E L T D F V L A I F I L L G P L S V T G											
670	*	680	*	690	*	700	*	710	*	720	*
GCA TCC TAC ATG GCC ATC ACA GGT GCT GTG ATG CGC ATC CCC TCA GCT GCT GGC CGC CAT											
A S Y M A I T G A V M R I P S A A G R H											
730	*	740	*	750	*	760	*	770	*	780	*
AAA GCC TTT TCA ACC TGT GCC TCC CAC CTC ACT GTT GTG ATC ATC TTC TAT GCA GCC AGT											
K A F S T C A A S H L T V V I I F Y A A S											
790	*	800	*	810	*	820	*	830	*	840	*
ATT TTC ATC TAT GCC AGG CCT AAG GCA CTC TCA GCT TTT GAC ACC AAC AAG CTG GTC TCT											
I F I Y A A R P K A A L S A F D T N K L V S											
850	*	860	*	870	*	880	*	890	*	900	*
GTA CTC TAC GCT GTC ATT GTA CCG TTG TTC AAT CCC ATC ATC TAC TGC TTG CGC AAC CAA											
PRONUC/TRA OPTION											
V L Y A V I V P L F N P I I Y C L R N Q											

Figure 14D

[illegible]

Translation begun with base no. 119

Translated to base no. 1102

Sequence printed from base no. 119 to base no. 1102

Sequence numbered beginning with base no. 119

Figure 15A Translated sequence of I8T.DLS

53/99

10	20	30	40	50	60
* ATG AAC AAC AAA ACT GTC ATC ACC CAT TTC CTC CTC CTG GGA TTG CCC ATC CCC CCA CAG	* M N N K T V I T H F L L L G L P I P P E	* 70	* 80	* 90	* 100
* CAC CAG CAA CTG TTC TTT GCC CTG TTC CTG ATC ATG TAC CTC ACC ACC TTT CTG GGA AAC	* H Q Q L F F A L F L I M Y L T T F L G N	* 130	* 140	* 150	* 160
* CTG CTA ATT GTT GTC CTT GTT CAA CTG GAC TCT CAT CTC CAC ACA CCC ATG TAC TTG TTT	* L L I V V L V Q L D S H L H T P M Y L F	* 190	* 200	* 210	* 220
* CTC AGC AAC TTG TCC TTC TCT GAT CTC TGC TGT TCC TCT TCC TCT GTT ACA ATG CTG AAA TTG CTC	* L S N L S F S D L C F S S S V T M L K L L	* 250	* 260	* 270	* 280
* CAA AAT ATA CAG AGC CAA GTA CCA TCT ATA TCC TAT GCA GGA TGC CTG ACA CAG ATA TTC	* Q N I Q S S Q V P S I S Y A G C L T Q I F				

Figure 15B

TTC TTT TTG TTG TTT GGC TAC CTT GGC AAT TTC CTT CTT GTA GCC ATG GCC TAT GAC CGC	310	320	330	340	350	360
F L L F G Y L L G N F L L L V A M A Y D R	*	*	*	*	*	*
TAT GTG GCC ATC TGC TTT TGC CCT CTT CTT CAT TAT ACC AAC ATC ATG AGC CAT AAG CTC TGT ACT	370	380	390	400	410	420
Y V A I C F F C T P L L H Y T N I M S H K L C T	*	*	*	*	*	*
IGT CTC CTG CTG GTA TTT TGG ATA ATG ACA TCA TCT CAT GCC ATG ATG CAC ACC CTG CTT	430	440	450	460	470	480
C L L L V F W I M T S S S H A M M H T L L	*	*	*	*	*	*
GCA GCA AGA TTG TCT TTT TGT GAG AAC AAT GTA CTC CTC AAC TTT TTC TGT GAC CTG TTT	490	500	510	520	530	540
A A R L L S F C E N N V L L L N F F C D L F	*	*	*	*	*	*
GTT CTC CTA AAG TTG GCC TGC TCA GAC ACT TAT GTT AAT GAG TTG ATG ATA CAT ATC ATG	550	560	570	580	590	600
V L L K L A C S D T Y V N E L M I H I M	*	*	*	*	*	*
	610	620	630	640	650	660

54/99

Figure 15C

[illegible]

56/99

Figure 15D

	910		920		930		9
	*		*		*		
AGA GTT ACC TGT AGC AAG AAA ATC TCT CTG CCA TGG TAG							
R V T C S K K I S L P W -							

Translation begun with base no. 57

Translated to base no. 995

Sequence printed from base no. 57 to base no. 995

Sequence numbered beginning with base no. 57

Figure 16A Translated sequence of I9T.D1S

10 * 20 * 30 * 40 * 50 * 60 *
 ATG ACT AGA AGA AAC CAA ACT GCC ATC TCT CAG TTC TTC CTT CTG GGC CTC CCA TTC CCC
 M T R R N Q T A I S Q F F L L G L P F P

 70 * 80 * 90 * 100 * 110 * 120 *
 GCA GAG TAC CAA CAC CTG TTC TAT GCC CTG TTC CTG GGC ATG ATG TAC CTC ACC ACT CTC CTC
 P E Y Q H L F Y A L F L A M Y L T T L L

 130 * 140 * 150 * 160 * 170 * 180 *
 GGG AAC CTC ATC ATC ATC CTC ATT CTA CTG GAC TCC CAT CTC CAC ACA CCC ATG TAC
 G N L I I I I L L L D S H L H T P M Y

 190 * 200 * 210 * 220 * 230 * 240 *
 TTG TTT CTC AGC AAT TTA TCC TTT GCC GAC CTC TGT TTT TCC TCT CTC ACA ATG CCC AAG
 L F L S N L S F A D L C F S S V T M P K

 250 260 270 280 290 300

57/99

Figure 16B

* * * * *
 TTG TTG CAG AAC ATG CAG AGC CAA GTT CCA TCC ATC CCC TAT GCA GGG TGC CTG GCA CAG
 L L Q N M Q S Q S Q V P S I P Y A G C L A Q *
 310 320 330 340 350 360
 * * * * *
 ATA TAC TTC TTT CTG TTT TTT GGA GAC CTT GGA AAC TTC CTG CTT GTG GCC ATG GCC TAT
 I Y F F L F F F G D L L G N F L L V A M A Y *
 370 380 390 400 410 420
 * * * * *
 GAC CGC TAT CTG GCC ATG TGC TTC CCC CTT CAT TAC ATG AGC ATC ATG AGC CCC AAG CTC
 D R Y V A I C F F P L H Y M S I M S P K L *
 430 440 450 460 470 480
 * * * * *
 TGT GTG AGT CTG GTG GTG CTG TCC TCG CTG CTG ACT ACC TTC CAT CAT GCC ATG CTG CAC ACC
 C V S L V V V L S W V L T T F H A M L H T *
 490 500 510 520 530 540
 * * * * *
 CTG CTC ATG GCC AGA TTG TCA TTC TGT GAG GAC AGT GTG ATC CCT CAC TAT TTC TGT GAT
 L L M A R L S F C E D S V I P H Y F C D *
 550 560 570 580 590 600
 * * * * *
 ATG TCT ACT CTG CTG AAA GTG GCT TGT TCT GAC ACC CAT GAT AAT GAA TTA GCA ATA TTT
 M S T L L K V A C S D T H D N E L A I F *

58/99

Figure 16C

	610	620	630	640	650	660													
AATC	TTA	GGG	GCC	CCT	ATA	GTT	GTA	CTA	CCT	TTC	TTT	CTC	ATC	ATT	GTT	TCT	TAT	GCA	AGA
I	L	G	G	P	I	V	V	L	P	F	L	L	I	I	V	S	Y	A	R
	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
	670	680	690	700	710	720													
AATT	GTT	TCC	TCC	ATC	TTC	AAG	GTC	CCT	TCT	TCT	CAA	AGC	ATC	CAT	AAA	GCC	TTC	TCC	ACC
I	V	S	S	I	F	K	V	P	S	S	Q	S	I	H	K	A	F	S	T
	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
	730	740	750	760	770	780													
TGT	GGC	TCC	CAC	CTG	TCT	GTG	GTG	TCA	CTG	TTC	TAT	GGG	ACA	GTC	ATT	GGT	CTC	TAC	TTA
C	G	S	H	L	S	V	V	S	L	F	Y	G	T	V	I	C	L	Y	L
	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
	790	800	810	820	830	840													
TGT	CCT	TCA	GCT	AAT	AAC	TCC	ACT	GTG	AAG	GAG	ACT	GTC	ATG	TCT	TTG	ATG	TAC	ACA	ATG
	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
	PRONUC/TRA	OPTION																	
C	P	S	A	N	N	S	T	V	K	E	T	V	M	S	L	M	Y	T	M

60/99

Figure 16D

850	*	860	*	870	*	880	*	890	*	900	*
GTG ACA CCC ATG CTG AAC CCC TTC ATC TAC AGC CTA AGA AAC AGA GAC ATA AAA GAT GCA											
V T P M L N P F I Y S L R N R D I K D A											
910	*	920	*	930	*	940	*				
TTA GAA AAA ATA ATG TGC AAA AAG CAA ATT CCC TCC TTT CTA TGA											
L E K I M C K K Q I P S F L -											

Translation begun with base no. 200

Translated to base no.1144

Sequence printed from base no. 200 to base no.1144

Sequence numbered beginning with base no. 200

Figure 17A Translated sequence of I14T.D1S

61/99

10	20	30	40	50	60
* ATG ACT GGA AAT AAC CAA ACT TTG ATC TTG GAG TTC CTC CTC GGT CTC CCC ATC CCA	* M T G N N Q T L I L E F L L L G L P I P	* 70	* 80	* 90	* 100
* TCA GAG TAT CAT CTC CTG TTC TAT GCC CTG TTC CTG GCC ATG TAC CTC ACC ATC ATC CTG	* S E Y H L L L F Y A L F L A M Y L T I I L	* 110	* 120	* 130	* 140
* GGA AAC CTG CTA ATC ATT GTC CTT GTT CGA CTG GAC TCT CAT CTC CAC ATG CCC ATG TAC	* G N L L I I V L V L R L D S H L L H M P M Y	* 150	* 160	* 170	* 180
* TTG TTT CTC AGC AAC TTG TCC TTC TCT GAC CTC TGC TGT TCC TCT GTC ACA ATG CCC AAA	* L F L S N L S F S D L C F S S V T M P K	* 190	* 200	* 210	* 220
* TTG CTT CAG AAC ATG CAG AGC CAA GTA CCA TCT ATA TCC TAT ACA GGC TGC CTG ACA CAG	* L L Q N M Q S S Q V P S I S Y T C C L T Q	* 230	* 240	* 250	* 260
* TTG CTT CAG AAC ATG CAG AGC CAA GTA CCA TCT ATA TCC TAT ACA GGC TGC CTG ACA CAG	* L L Q N M Q S S Q V P S I S Y T C C L T Q	* 270	* 280	* 290	* 300

63/99

Figure 17C

ATC	TTG	GGT	GGA	CTC	ATC	ATT	ATT	ATC	CCA	TTC	CTA	TTA	ATT	GTT	ATG	TCC	TAT	GTT	AGA	*
I	L	G	G	L	I	I	I	I	P	F	L	L	I	V	M	S	Y	V	R	*
670						680			690			700				710			720	
*						*			*			*				*			*	
ATT	TTC	TTC	TCC	ATT	TTG	AAG	TTT	CCA	TCT	ATT	CAG	GAC	ATC	TAC	AAG	GTA	TTC	TCA	ACC	
I	F	F	S	I	L	K	F	P	S	I	Q	D	I	Y	K	V	F	S	T	
730						740			750			760				770			780	
*						*			*			*				*			*	
TGT	GGT	TCC	CAT	CTG	TCT	GTG	ACC	TTC	TTG	TTT	TAT	GGG	ACA	ATT	TTT	GGT	ATC	TAC	TTA	
C	G	S	H	L	S	V	V	T	L	F	Y	G	T	I	F	G	I	Y	L	
790						800			810			820				830			840	
*						*			*			*				*			*	
TGT	CCA	TCA	GGT	AAT	AAT	TCT	ACT	CTG	AAG	GAG	ATT	GCC	ATG	GCT	ATG	ATG	TAC	ACA	CTC	
PRONUC/TRA OPTION																				
C	P	S	G	N	N	S	T	V	K	E	I	A	M	A	M	M	Y	T	V	
850						860			870			880				890			900	
*						*			*			*				*			*	
GTG	ACT	CCC	ATG	CTG	AAT	CCC	TTC	ATC	TAC	AGC	CTG	AGG	AAC	AGA	GAC	ATG	AAA	AGG	GCC	
V	T	P	M	L	N	P	F	I	Y	S	L	R	N	R	D	M	K	R	A	

64/99

Figure 17D

	910		920		930		9
	*		*		*		
CTA	ATA	AGA	GTT	ATC	TGC	ACT	AAG
L	I	R	V	I	C	T	K
							K
							I
							S
							L
							-
							TAA

Translation begun with base no. 64

Translated to base no.1002

Sequence printed from base no. 64 to base no.1002

Sequence numbered beginning with base no. 64

Figure 18A Translated sequence of I15T.D1S

65/99

10	20	30	40	50	60
* ATG ACA GAA GAG AAC CAA ACT GTG ATC TCC CAG TTC CTT CTC CTT TTC CTG CCC ATC CCC	* M T E E N Q T V I S Q F L L L L F L P I P	* 70	* 80	* 90	* 100
* TCA GAG CAC CAC GTG TTC TAC GCC CTG TTC CTG TCC TCC ATG ATG TAC CTC ACC ACT CTC CTC	* S E H Q C H V F Y A L F L S M Y L T T V L	* 130	* 140	* 150	* 160
* GGG AAC CTC ATC ATC ATC CTC ATT CAC CTG GAC TCC CAT CTC CAC ACA CCC ATG TAC	* G N L I I I I L I H L D S H L L H T P M Y	* 190	* 200	* 210	* 220
* TTG TTT CTC AGC AAC TTG TCC TTC TCT GAT CTC TGC TGC TTT TCC TCT TCT GTT ACG ATG CCC AAG	* L F L S N L S F S D L C F S S V T M P K	* 250	* 260	* 270	* 280
* TTG TTG CAG AAC ATG CAG ACC CAA GTT CCA TCC ATC CCC TTT GCA GGC TGC CTG ACA CAA	* 300				

66/99

Figure 18B

310	320	330	340	350	360
* TTA TAC TTT TAC CTG TAT TTT GCA GAC CTT GAG AGC TTC CTG CTT GTG GCC ATG GCC TAT					
L Y F Y L Y L Y F A D L E S F L L L V A M A Y					
370	380	390	400	410	420
* GAC CGC TAT GTG GCC ATC TGC TTC CCC CTT CAT TAC ATG AGC ATC ATG AGC CCC AAG CTC					
D R Y V A I C F P L H Y M S I M S P K L					
430	440	450	460	470	480
* TGT GTG AGT CTG GTG CTG TCC TGG GTG CTG ACC ACC TTC CAT CCC ATG CTG CAC ACC					
C V S L V V L S W V L T T F H A M L H T					
490	500	510	520	530	540
* CTG CTC ATG GCC AGA TTG TCA TTC TGT GCG GAC AAT ATG ATC CCC CAC TTT TTC TGT CAT					
L L M A R L L S F C A D N M I P H F C D					
550	560	570	580	590	600
* ATA TCT CCT TTA TTG AAA CTG TCC TGC TCT GAC ACC CAT GTT AAT GAG TTG GTG ATA TTT					
I S P L L K L S C S D T H V N E L V I F					
610	620	630	640	650	660

67/99

Figure 18C *

GTC	ATG	GGA	GGG	CTT	GTT	ATT	GTC	ATT	CCA	TTT	GTG	CTC	ATC	ATT	GTA	TCT	TAT	GCA	CGA	*
V	M	G	G	L	V	I	V	I	P	F	V	L	I	I	V	S	Y	A	R	
670						680			690				700			710			720	*
GTT	CTC	GCC	TCC	ATT	CTT	AAA	GTC	CCT	TCT	GTC	CGA	GGC	ATC	CAC	AAG	ATC	TTC	TCC	ACC	*
V	V	A	S	I	L	K	V	P	S	V	R	G	I	H	K	I	F	S	T	
730						740			750				760			770			780	*
TGC	GGC	TCC	CAT	CTG	TCT	GTC	GTC	TCA	CTG	TTC	TAT	GGG	ACA	ATC	ATT	GGT	CTC	TAC	TTA	*
C	G	S	H	L	S	V	V	S	L	F	Y	G	T	I	I	G	L	Y	L	
790						800			810				820			830			840	*
TGT	CCG	TCA	GCT	AAT	AAC	TCT	ACT	GTC	AAG	GAG	ACT	GTC	ATG	GCC	ATG	ATG	TAC	ACA	GTG	*
PRONUC/TRA OPTION																				
C	P	S	A	N	N	S	T	V	K	E	T	V	M	A	M	M	Y	T	V	
850						860			870				880			890			900	*
GTG	ACC	CCC	ATG	CTG	AAC	CCC	TTC	ATC	TAC	AGC	CTG	AGG	AAC	AGA	GAC	ATG	AAA	GAG	GCA	*
V	T	P	M	L	N	P	F	I	Y	S	L	R	N	R	D	M	K	E	A	

Figure 18D

	910	920	930	940
CTG ATA AGA GTC CTT TGT AAA AAG AAA ATT ACC TTC TGT CTA TGA	*	*	*	*
L I R V L C K K K I T F C L -				

Translation begun with base no. 8
Translated to base no. 952
Sequence printed from base no. 8 to base no. 952
Sequence numbered beginning with base no. 8

69/99

Figure 19A

Translated Sequence of H5.D1S

10					20				
ATC	TGT	TTT	GTG	TCT	ACC	ACT	GTC	CCA	
I	C	F	V	S	T	T	V	P	
70					80				
*					*				
GTC	ATC	AAC	TAT	GCA	GAC	TGC	ATC	ACC	
V	I	T	Y	A	D	C	I	T	
*					*				
GAC	AGC	TTA	CTC	CTG	ACT	GTG	ATG	GCC	
D	S	L	L	L	T	V	M	A	
190					200				
*					*				
CAC	TAC	ACA	GTC	ATT	ATG	AGC	TCC	TGG	
H	Y	T	V	I	M	S	S	W	
250					260				
*					*				
GTG	AGC	ATC	CTA	TAT	TCT	CTG	TTA	CAA	
V	S	I	L	Y	S	L	L	Q	

70/99

Figure 19B

30		40		50		60				
*		*		*		*				
AAG	CAG	CTG	GTG	AAC	ATC	CAG	ACA	CAG	AGC	AGA
K	Q	L	V	N	I	Q	T	Q	S	R
90		100		110		120				
*										
CAG	ATG	TGC	TTT	TTT	ATA	CTC	TTT	GTA	GTG	TTG
Q	M	C	F	F	I	L	F	V	V	L
		160		170		180				
*		*		*		*				
TAT	GAC	CGG	TTT	GTG	GCC	ATC	TGT	CAC	CCC	CTG
Y	D	R	F	V	A	I	C	H	P	L
210		220		230		240				
*		*		*		*				
CTC	TGT	GGA	CTG	CTG	GTT	CTG	GTG	TCC	TTG	ATC
L	C	G	L	L	V	L	V	S	N	I
270		280		290		300				
*		*		*		*				
AGC	ATA	ATG	GCA	TTG	CAG	CTG	TCC	TTC	TGT	ACA
S	I	M	A	L	Q	L	S	F	C	T

71/99

Figure 19C

310 *	320 *	330 *
GAA CTG AAA ATC CCT CAA TTT TTC TGT GAA		
E L K I P Q F F C E		
370 *	380 *	390 *
GAC ACT TTT ATT AAT GAC ATG ATG ATG AAT		
D T F I N D M M M N		
430 *	440	450 *
CTC GCT GGA ATA TTT TAC TAC TTT AAG		
L A G I F Y X Y F K		
490 *	500 *	510 *
GCT CAG GGG ATG AAT AAA GCA CTT TCC ACC		
A Q G M N K A L S T		
550	560 *	570 *
TTT TAT TGT ACA GGC GTA GGT GTG TAC CTT		
F Y C T G V G V Y L		
610 *	620 *	630 *
AAT GCT GCA GCC TCG GTG ATG TAC ACT GTG		
N A A A S V M Y T V		

72/99
Figure 19D

340		350		360
*		*		*
CTT AAT CAG GTC ATC CAC CTT GCC TGT TCC				
L N Q V I H L A C S				
400		410		420
*		*		*
TTT ACA AGT GTG CTG CTG GGT GGG GGA TGC				
F T S V L L G G G C				
460		470		480
*		*		*
ATA CTT TGT TGC ATA TGT TCG ATC TCA TCA				
I L C C I C S I S S				
520		530		540
*		*		*
TGT GCA TCT CAC CTC TCA GTT GTC TCC TTA				
C A S H L S V V S L				
580		590		600
*		*		*
AGT TCT GCT GCA ACC CAT AAC TCA CTC TCA				
S S A A T H N S L S				
640				
*				
GTC ACC TCC ATG CTG				
V T S M L				

73/99

Figure 20A

J1

```

1  CATCTGCTTACTTCTGCTAGCATCCCAAGATGCTAGTGAATATACAGACGAAGACAA  +60
   I C F T S A S I P R M L V N I Q T K N K -
61  GGTGATCACCTATGAAGGCTGCATCTCCCAAGTATACTTTTCATACTCTTTCGAGTTTC
   V I T Y E G C I S Q V Y F S Y S L E F W -
121 GACAACTTCTTCTCGACTGTGATGGCCTATGACCGATATGTGCCCATCTGTCACCCATC
   T T F F S T V M A Y D R Y V A I C H P S -
181 TXACTACAGGTCATCATGAACCCXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXX
   ? Y T G H H E P ? ? ? ? ? ? ? ? ? ? ? ? ? ? ? ? ? ? -240

```

74/99

Figure 20B

XX
241 -----+-----+-----+-----+-----+-----+-----+300
?
-
XX
301 -----+-----+-----+-----+-----+-----+-----+360
?
-
XX
361 -----+-----+-----+-----+-----+-----+-----+420
?
-
XXXXXXXXXXTTTACTCTAAGATAGTTTCCTCCATACGAGAAATCTCATCATCACA
421 -----+-----+-----+-----+-----+-----+-----+480
? ? ? ? Y S Y S K I V S S I R E I S S S Q -
-
GGGAAGTACAAGXXATTCTCCACCTGTGCATCCACCTCTCAGTTGTTTCATTCTA
481 -----+-----+-----+-----+-----+-----+-----+540
G K Y K ? P S T C A S H L S V V S L F Y -
-

75/99

Figure 20C

541 TTCTACACTTTGGGTGCTACCTTAGTCTCTTCCTTACCCAAACTCACACTCAACTGC
-----+-----+-----+-----+-----+-----+-----+600
S T L L G V Y L S S S F T Q N S H S T A -

601 ACGGCCAICTGTTATGTACAGTGTGGTCACCCCATGTTG
-----+-----+-----+-----+-----+-----+ 640
R A S V M Y S V V T P M L -

76/99

Figure 21A

1 ACCTCCACCACCATCCCAAGATGCTGTAAATATACACACCCAGACCAATACTATCACC
T S T T I P K M L V N I H T Q S N T I T - 60
61 TATGAAGACTGTATTCCAGATGTTGTACTCTTGGTATTGGAGAACTGGACAACTTT
Y E D C I S Q M F V L L V F C E L D N F - 120
121 CTCCTGGCTGATGGCCTATGATCGATATGTTGGCTATCTGTCACCCACTGTATTACACA
L L A V M A Y D R Y V A I C H P L Y Y T - 180
181 GTCATGTGAACCAACGACTCTGTATCTCTGCTCTCTGCTCTGCTGGGTGTCAGCATTT
V I V N H R L C I L L L L L L S W V V S I - 240
241 TTACATGCCCTTCTTACAGAGCTTAATTGTACTACAGTTGACCTTCTGTGGAGATGTGAAA
L H A F L Q S L I V L Q L T F C G D V K - 300

J2

Figure 21B

ATCCCTCACTTCTCTGTGAGCTCAATCAGCTGTCCCAACTCACATGTTTCAGACAACTTT
301 I P H F F C E L N Q L S Q L T C S D N F - +360

CCAAGTCACCTCACAAATGCATCTGTGTACCTGTATTATTTGCAGCTATTTCCCTCAGTCGT
361 P S H L T M H L V P V I F A A I S L S G - +420

ATCCTTTACTCTTATTTC AAGATAGTGTCTTC CATACGTTCTATGTCTCAGTTCAACGG
421 I L Y S Y F K I V S S I R S M S S V Q G - +480

AAGTACAAGGCATTTTCTACATGTGCGCTCTCACCTTTCCATTGTCTCCTTATTTTATAGT
481 K Y K A F S T C A S H L S I V S L F Y S - +540

ACAGGCCTCGGGGTACGTCAGTTCTGTGTGATCCGAAGCTCACACTCTCTCTCCAAGT
541 T G L G V Y V S S A V I R S S H S S A S - +600

GCTTCGGTCATGTATACGTGGTCACCCCATGTTG
601 A S V M Y T V V T P M L - 636

78/99

Figure 22A

1 CATAGCGTATTTCATCTTCTGTGCACACCCAAATATGCTGTGTCAACTTCCTTATTAAGCAAA + 60
 I G Y S S V T P N M L V N F L I K Q N -
 61 TACCATCTCATACCTTGGATGTTCTATACAGTTTGGCTCAGCTGCTTGTGTTGGAGCTCT + 120
 T I S Y L G C S I Q P G S A A L F G G L -
 121 TGAATGCTTCTTCTGGCTGCCATGGCGTATGATCGTTTGTAGCAATCTGCAACCCACT + 180
 E C F L L A A M A Y D R F V A I C N P L -
 181 GCTTTATTCAACGAAATGTCCACACAACTCTGTGTCCAGTTGTTGGGATCTTATAT + 240
 L Y S T K M S T Q V C V Q L V V G S Y I -
 241 AGGGGGATTCTTAATGCCCTCCTCTTTTACCCTTTCCTTTTTCCTTGTCTCTGTGG + 300
 G G F L N A S S F T L S F F S L S F C G -

79/99

Figure 22B

```
ACCAATAGAAATCAACTTTACTGTGATTTTGCTCCGTTAGTAGAACTTTCTTGCTC
301 -----+-----+-----+-----+-----+-----+360
      P N R I N H F Y C D F A P L V E L S C S -
TGATGTCAGTGTTCCTGATGCTGTACCTCATTTTCTGCTGCCCTCAGTTACTATGCTCAC
361 -----+-----+-----+-----+-----+-----+420
      D V S V P D A V T S F S A A S V T M L T -
AGTGTTTATCATAGCCATCTTCCTATACCTATATCCTCATCACCATCCTGAAGATGCCGTTT
421 -----+-----+-----+-----+-----+-----+480
      V F I I A I S Y T Y I L I T I L K M R S -
CACTGAGGGTGCACAGAAAGCATTTCTGTACCTGCACCTTCCACCTCACTGCAGTCACTCT
481 -----+-----+-----+-----+-----+-----+540
      T E G R Q K A F S T C T S H L T A V T L -
GTGCTATGGAACCATCACATTCATCTATGTGATGCCCAAGTCCAGCTACTCCACAGACCA
541 -----+-----+-----+-----+-----+-----+600
      C Y C T I T F I Y V M P K S S Y S T D Q -
GAACAAGGTGGTCTCTGTTTATATAGGTGGTGATCCCATGTTG
601 -----+-----+-----+-----+-----+-----+646
      N K V V S V F Y M V V I P M L -
```

Figure 23A

1 CATCTGCCAAGCCCTGCTACTACACCACCACCATCATGAATAACCGAGTGTCACAGTTCTAGT
I C K P L H Y T T I M N N R V C T V L V - 60
61 CCTCTCCTGTGGTGGCTGGCTGGATCATCTCTCCACCTCTTGGTCATGGCCCTCCA
L S C W F A G L L I I L P P L G H G L Q - 120
121 GCTGGAGTTCGTGACTCCAAATGTGATMGATCATTTTGGCTGTGATGCCCTCTCCAAATTC
L E P C D S N V I D H F G C D A S P I L - 180
181 GCAGATAACCTGCTCAGACACCGTATTATAGAGAAATTTGTCTTGGCTTTTGCCATACT
Q I T C S D T V F I B K I V L A F A I L - 240
241 GAACTCATCATTAATCTGGTATGTGTGTTCTCTCTCTACACATACATCATCAAGACCAT
-----+-----+-----+-----+-----+-----+-----+300

80/99

J7

82/99

Figure 24A

```

1  CATCTGCCACCCGGCTCCACTACTCTCTCTCATGAGTCCTGACAACTGTGCTGCTCTGGT
   I C H P L H Y S L L M S P D N C A A L V - 60
61  AACAGTCTCTGGGTGACACGGGTGGCACCAGGCTTCTGCTTCCCTCCTGATTCTAA
   T V S W V T G V G T G F L P S L L I S K - 120
121 GTTGGACTTCTGTGGGCCCAACCGCATCAACCATTTCTTCGTGACCTCCCTCCATTAAAT
   L D F C G P N R I N H F F C D L P L I - 180
181 CCAGCTGTCTGCTCCAGCGTCTTTGTGACAGAAATGGCCATCTTTGTCTGTCCATCCG
   Q L S C S S V F V T E M A I F V L S I A - 240

```

J8

83/99

Figure 24B

241 TGTGCTCTGCATCTGTTTCCTCCTAACCCXXXXTCTCATATTTCATAGTCTCCTCCAT
-----+-----+-----+-----+-----+300
V L C I C F L L T ? ? S Y I F I V S S I -

301 TCTGAGAAATCCCTTCCACTACCCGCAGGATGAAGACATTTTCTACATGTGGCTCCACCT
-----+-----+-----+-----+-----+360
L R I P S T T G R M K T F S T C G S H L -

361 GGCCGTGGTCACCATCTACTATCGGACCATGATCTCTCCATGTATGTCCGCCCAATGCCCA
-----+-----+-----+-----+-----+420
A V V T I Y Y G T M I S M Y V G P N A H -

421 TCTGTCCCGAGCTCAACAAGGTCAATTCTGTCTTCTACACTGTGATCACCCCACTACT
-----+-----+-----+-----+-----+480
L S P E L N K V I S V F Y T V I T P L L -

G
481 - 481

67/98

Figure 18C

GTC	ATG	GGA	GGG	CTT	GTT	ATT	CTC	ATT	CCA	TTT	GTG	CTC	ATC	ATT	GTA	TCT	TAT	GCA	CGA	*
V	M	G	G	L	V	I	V	I	P	F	V	L	I	I	V	S	Y	A	R	*
670						680			690							710			720	
*						*			*							*			*	
GTT	GTC	GGC	TCC	ATT	CTT	AAA	GTC	CCT	TCT	GTC	CGA	GGC	ATC	CAC	AAG	ATC	TTC	TCC	ACC	
V	V	A	S	I	L	K	V	P	S	V	R	G	I	H	K	I	F	S	T	
730						740			750							770			780	
*						*			*							*			*	
TGC	GGC	TCC	CAT	CTG	TCT	GTC	GTG	TCA	CTG	TTC	TAT	GGG	ACA	ATC	ATT	GGT	CTC	TAC	TTA	
C	G	S	H	L	S	V	V	S	L	F	Y	G	T	I	I	G	L	Y	L	
790						800			810							830			840	
*						*			*							*			*	
TGT	CCG	TCA	GCT	AAT	AAC	TCT	ACT	GTG	AAG	GAG	ACT	GTC	ATG	GCC	ATG	ATG	TAC	ACA	GTG	
PRONUC/TRA						OPTION														
C	P	S	A	N	N	S	T	V	K	E	T	V	M	A	M	M	Y	T	V	
850						860			870							890			900	
*						*			*							*			*	
TG	ACC	CCC	ATG	CTG	AAC	CCC	TTC	ATC	TAC	AGC	CTG	AGG	AAC	AGA	GAC	ATG	AAA	GAG	GCA	
V	T	P	M	L	N	P	F	I	Y	S	L	R	N	R	D	M	K	E	A	

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Figure 18D

	910		920		930		940
	*		*		*		*
CTC ATA AGA GTC CTT TGT AAA AAG AAA ATT ACC TTC TGT CTA TGA							
L I R V L C K K K I T F C L -							

Translation begun with base no. 8

Translated to base no. 952

Sequence printed from base no. 8 to base no. 952

Sequence numbered beginning with base no. 8

FIGURE 19

FIGURE 19A

FIGURE 19B

FIGURE 19C

FIGURE 19A

Translated Sequence of H5.D1S

10			Tm2			20			30		
*						*			*		
ATC	TGT	TTT	GTG	TCT	ACC	ACT	GTC	CCA	AAG	CAG	
I	C	F	V	S	T	T	V	P	K	Q	
40			50			60					
*			*			*					
CTG	GTG	AAC	ATC	CAG	ACA	CAG	AGC	AGA	GTC	ATC	
L	V	N	I	Q	T	Q	S	R	V	I	
70			80			90			Tm3		
*			*			*			*		
ACC	TAT	GCA	GAC	TGC	ATC	ACC	CAG	ATG	TGC	TTT	
T	Y	A	D	C	I	T	Q	M	C	F	
110			120			130					
*			*			*					
TTT	ATA	CTC	TTT	GTA	GTG	TTG	GAC	AGC	TTA	CTC	
F	I	L	F	V	V	L	D	S	L	L	
140			HaeIII			P1			160		
*			*			*			*		
CTG	ACT	GTG	ATG	GCC	TAT	GAC	CGG	TTT	GTG	GCC	
L	T	V	M	A	Y	D	R	F	V	A	
170			P9			180			190		
*			*			*			*		
ATC	TGT	CAC	CCC	CTG	CAC	TAC	ACA	GTC	ATT	ATG	
I	C	H	P	L	H	Y	T	V	I	M	
200			210			220			Tm4		
*			*			*			*		
AGC	TCC	TGG	CTC	TGT	GGA	CTG	CTG	GTT	CTG	GTG	
S	S	W	L	C	G	L	L	V	L	V	

FIGURE 19B

240			250			260				
*			*			*				
TCC	TTG	ATC	GTG	AGC	ATC	CTA	TAT	TCT	CTG	TTA
S	W	I	V	S	I	L	Y	S	L	L
270			280			290				
*			*			*				
CAA	AGC	ATA	ATG	GCA	TTG	CAG	CTG	TCC	TTC	TGT
Q	S	I	M	A	L	Q	L	S	F	C
300			310			320			330	
*			*			*			*	
ACA	GAA	CTG	AAA	ATC	CCT	CAA	TTT	TTC	TGT	GAA
T	E	L	K	I	P	Q	F	F	C	E
340			350			360				
*			*			*				
CTT	AAT	CAG	GTC	ATC	CAC	CTT	GCC	TGT	TCC	GAC
L	N	Q	V	I	H	L	A	C	S	D
370			380			Tm5			390	
*			*						*	
ACT	TTT	ATT	AAT	GAC	ATG	ATG	ATG	AAT	TTT	ACA
T	F	I	N	D	M	M	M	N	F	T
400			410			420			430	
*			*			*			*	
AGT	GTG	CTG	CTG	GGT	GGG	GGA	TGC	CTC	GCT	GGA
S	V	L	L	G	G	G	C	L	A	G
440			450			460				
*			*			*				
ATA	TTT	TAC	T--	TAC	TTT	AAG	ATA	CTT	TGT	TGC
I	F	Y	X	Y	F	K	I	L	C	C
470			480			490				
*			*			*				
ATA	TGT	TCG	ATC	TCA	TCA	GCT	CAG	GGG	ATG	AAT
I	C	S	I	S	S	A	Q	G	M	N

FIGURE 19C

	500		510		Tm6		520				
	*		*				*				
AAA	GCA	CTT	TCC	ACC	TGT	GCA	TCT	CAC	CTC	TCA	
K	A	L	S	T	C	A	S	H	L	S	
530			540			550				560	
*			*			*				*	
GTT	GTC	TCC	TTA	TTT	TAT	TGT	ACA	GGC	GTA	GGT	
V	V	S	L	F	Y	C	T	G	V	G	
		570			580				590		
		*			*				*		
GTG	TAC	CTT	AGT	TCT	GCT	GCA	ACC	CAT	AAC	TCA	
V	Y	L	S	S	A	A	T	H	N	S	
	600			610		Tm7		620			
	*			*				*			
CTC	TCA	AAT	GCT	GCA	GCC	TCG	GTG	ATG	TAC	ACT	
L	S	N	A	A	A	S	V	M	Y	T	
630			640								
*			*								
GTG	GTC	ACC	TCC	ATG	CTG						
V	V	T	S	M	L						

FIGURE 20

FIGURE 20A
FIGURE 20B
FIGURE 20C

FIGURE 20A

J1

Tm2

```

1  CATCTGCTTTACTTCTGCTAGCATCCCAAAGATGCTAGTGAATATACAGACGAAGAACAA 60
   I C F T S A S I H K M L V N I Q T K N K -
61  GGTGATCACCTATGAAGGCTGCATCTCCCAAGTATACTTTTCATACTCTTTGGAGTTTG 120
   V I T Y E G C I S Q V Y F S Y S L E F W -
121 GACAACTTTCTCTCGACTGTGATGGCCTATGACCGATATGTGGCCATCTGTCACCCATC 180
   T T F F S T V M A Y D R Y V A I C H P S -
181 TXACTACACAGGTCATCATGAACCCXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXX 240
   ? Y T G H H E P ? ? ? ? ? ? ? ? ? ? ? ? ? ? ? ? ? ? ? ? ? ?

```


FIGURE 20C

```
421 XXXXXXXTTTATTCTTACTCTAAGATAGTTTCTCTCCATACGAGAAATCTCATCATCACA 480
    ? ? ? Y S Y S K I V S S I R E I S S S Q -
481 GGGAAAGTACAAGXXATCTCTCCACCTGTGCATCCACCTCTCAGTTGTTTCATTATCTA 540
    G K Y K ? F S T C A S H L S V V S L F Y -
541 TTCTACACTTTTGGGTGTACCTTAGTTCTTCTTTTACCCAAAACCTCACACTCAACTGC 600
    S T L L G V Y L S S S F T Q N S H S T A -
601 ACGGCATCTGTTATGTACAGTGTGGTCACCCCATGTTG 640
    R A S V M Y S V V T P M L -
```


FIGURE 21

FIGURE 21A

FIGURE 21B

FIGURE 21A

Tm2

1	ACCTCCACCACCATCC	AAAGATGCTGTAAATATACACACCCAGAGCAATACTATCACC	60
	T S T T I P K M L V N I H T Q S N T I T	-	
60	TATGAAGACTGTATTCC	CAGATGTTTGTACTCTTGGTTTTTGGAGAACTGGACAACTTT	120
	Y E D C I S Q M F V L L V F G E L D N P	-	
121	CTCCTGGCTGTGATGGCCTATGATCGATATGTGGCTATCTGTCA	CCCCACTGTATTACACA	180
	L L A V M A Y D R Y V A I C H P L Y Y T	-	
181	GTCATTGTGAACCA	CCGACTCTGTATCCTGTCTCTGTCTGCTGGTGTGCAGCAAT	240
	V I V N H R L C I L L L L L S W V S I	-	
241	TTACATGCCTTCTTACAGAGCTTAATTGTACTACAGTTGACCTTCTGTGGAGATGTGAA	-	300
	L H A F L Q S L I V L Q L T F C G D V K	-	

FIGURE 22

FIGURE 22A

FIGURE 22B

FIGURE 22A

J4

Tm2

```

CATAGGCTATTCACTCTCTGTCAACCCCAATATGCTGTCAACTTCCTTATAAAGCAAAA
1  -----+-----+-----+-----+-----+-----+-----+
  I  G  Y  S  S  S  V  T  P  N  M  L  V  N  F  L  I  K  Q  N  -  60
TACCATCTCATACCTTGGATGTTCTATACAGTTTGGCTCAGCTGCTTTGTTGGAGGTCT
61 -----+-----+-----+-----+-----+-----+-----+
  T  I  S  Y  L  G  C  S  I  Q  F  G  S  A  A  L  F  G  G  L  -  120
TGAATGCTTCCTTCTGGCTGCCATGGCGTATGATCGTTTGTAGCAATCTGCAACCCACT
121 -----+-----+-----+-----+-----+-----+-----+
  E  C  F  L  L  A  A  M  A  Y  D  R  F  V  A  I  C  N  P  L  -  180
GCTTTATTCAACGAAATGTCCACACAAGTCTGTGTCCAGTTGGTGTGGGATCTTATAT
181 -----+-----+-----+-----+-----+-----+-----+
  L  Y  S  T  K  M  S  T  Q  V  C  V  Q  L  V  V  G  S  Y  I  -  240
AGGGGATTTCTTAATGCCCTCCCTCTTTACCCCTTTCCTTTTTCCTTGTCTCTGTGG
241 -----+-----+-----+-----+-----+-----+-----+
  G  G  F  L  N  A  S  S  F  T  L  S  F  F  S  L  S  F  C  G  -  300

```

FIGURE 22B

301 ACCAAATAGAAATCAATCACTTTTACTGTGATTTTGCTCCGTTAGTAGAACTTCTTGCTC 360 -
P N R I N H F Y C D F A P L V E L S C S
361 TGATGTCAGTGTCTGATGCTGTACCTCATTTTCTGCTGCCCTCAGTTACTATGCTCAC 420 -
D V S V P D A V T S F S A A S V T M L T
421 AGTGTTTATCATAGCCATCTCCTATACCTATATCCTCATCACCATCCTGAAGATGCGTTC 480 -
V F I I A I S Y T Y I L I T I L K M R S
481 CACTGAGGGTCGACAGAAAGCATTTCTCTACCTGCACCTTCCCACCTCACTGCAGTCACTCT 540 -
T E G R Q K A F S T C T S H L T A V T L
541 GTGCTATGGAACCATCACAATTCATCTATGTGATGCCCAAGTCCAGCTACTCCACAGACCA 600 -
C Y G T I T F I Y V M P K S S Y S T D Q
601 GAACAAGGTGGTGTCTGTGTTTATATGGTGGTGATCCCCATGTTG 646 -
N K V V S V F Y M V V I P M L

FIGURE 23

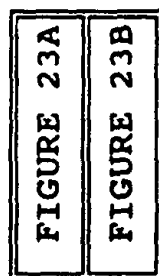


FIGURE 23A

J7

Tm4

```

1  CATCTGCAAGCCCTGCACTACACCACCATCATGAATAACCGAGTGTGCACAGTTCTAGT 60
   I C K P L H Y T T I M N N R V C T V L V -
61  CCTCTCCTGTGGTTTGCTGGCCTGTGATCATCCTCCACCTCTTGGTCATGGCCTCCA 120
   L S C W F A G L L I I L P P L G H G L Q -
121 GCTGGAGTTCTGTGACTCCAATGTGATGATCATTTTGGCTGTGATGCCCTCTCCAATTCT 180
   L E F C D S N V I D H F G C D A S P I L -
181 GCAGATAACCTGCTCAGACACGGTATTTATAGAGAAATGTCTTGGCTTTTGCCATACT 240
   Q I T C S D T V F I E K I V L A F A I L -
241 GACACTCATTACTCTGGTATGTGTGTTCTCTCCTACACATACATCATCAAGACCAT 300
   T L I I T L V C V V L S Y T Y I I K T I

```

FIGURE 23B

```
301      TTTAAAGTTTCCTTCGTCAACAAGAAAAAGGCCCTTTTCTACATGTTCTTCCCACAT      360
      -----+-----+-----+-----+-----+-----+-----+
      L K F P S A Q Q R K K A F S T C S S H M
      -----+-----+-----+-----+-----+-----+-----+

361      GATTGTGGTTTCCCATCACCTATGGGAGCTGTATTTTCATCTACATCAAAACCTTCAGCGAA      420
      -----+-----+-----+-----+-----+-----+-----+
      I V V S I T Y G S C I F I Y I K P S A K
      -----+-----+-----+-----+-----+-----+-----+

421      GGAAGGGTAGCCCATCAATAAGGTTGTATCTGTGCTCACAAACATCAGTCGCCCCCTTTGCT      480
      -----+-----+-----+-----+-----+-----+-----+
      E G V A I N K V V S V L T T S V A P L L
      -----+-----+-----+-----+-----+-----+-----+

      C
481      - 481
      G
```

FIGURE 24

FIGURE 24A

FIGURE 24B

FIGURE 24A

85

[illegible]

FIGURE 24B

```
241 TGTGCTCTGCATCTGTTTCCTCCTAACCXXXTCCTACATTTTCATAGTGTCTCCAT 300 -  
-----+-----+-----+-----+-----+-----+-----+  
V L C I C F L L T ? ? S Y I F I V S S I  
301 TCTGAGAAATCCCTTCCACTACCGGCAGGATGAAGACATTTTCTACATGTGGCTCCACCT 360 -  
-----+-----+-----+-----+-----+-----+-----+  
L R I P S T T G R M K T F S T C G S H L  
361 GGCCGTGGTCACCATCTACTATGGGACCATGATCTCCATGTATGTGGCCCAAATGCGCA 420 -  
-----+-----+-----+-----+-----+-----+-----+  
A V V T I Y Y G T M I S M Y V G P N A H  
421 TCTGTCCCCGGAGCTCAACAAGGTCATTTCTGTCTTCTACACTGTGTGATCACCCCACTACT 480 -  
-----+-----+-----+-----+-----+-----+-----+  
L S P E L N K V I S V F Y T V I T P L L  
G  
481 - 481
```


FIGURE 25B

301 XX 360 -
-----+-----+-----+-----+-----+-----+-----+
?
361 XXXTGTGATCATGGTCACCCC 420 -
-----+-----+-----+-----+-----+-----+-----+
?
421 ATTTGTGTCATCCTCATCTCTTACATCTACATCACCACCAATGCAGTCCTCAGAGTCTCATC 480 -
-----+-----+-----+-----+-----+-----+-----+
F V C I L I S Y I Y I T N A V L R V S S
481 CTTTAGGGAGGATGGAAAGCCTTCTCCACCTGTGGCTCACACCTGGCTGTGGTCTGCCT 540
-----+-----+-----+-----+-----+-----+-----+
F R G G W K A F S T C G S H L A V V C L

FIGURE 25C

```
541 CTTCTATGGCACCATCATTTGCTGTGTAATTTCAATCCTGTATCTTCCCATTCATCTGAGAA 600
    F Y G T I I A V Y F N P V S S H S S E K -
601 GGACACTGCAGCAACTGTGCTATACACAGTGGTGA CTCCCATGTTG 646
    D T A A T V L Y T V V T P M L -
```

FIGURE 26

FIGURE 26A

FIGURE 26B

FIGURE 26A

J14 Tm2 April 4, 1992 22:46

1 TGTCTGCTTCTCCTCCACCACTGTCCCAAGTACTGGCTAACCATACACTCAGTAGTCA 60
V C F S S T T V P K V L A N H I L S S Q -

61 GGCCATTTCCTTCTCTGGGTGCTAACTCAGCTGTATTTTCTCTGTGTCTGTGAATAT 120
A I S F S G C L T Q L Y F L C V S V N M

121 GGACAAATTTCCTGCTGGCTGTGATGGCCCTATGACAGATTGTGGCCATATGCCACCCCTTT 180
D N F L L A V M A Y D R F V A I C H P L -

181 GTACTACACAACAAGATGACCCACCACTCTGTGTCTGTGTGTGTGGATCAXXXXXX 240
Y Y T T K M T H Q L C V L L V S G S ? ?

241 XXX 300
? ?

FIGURE 27

FIGURE 27A

FIGURE 27B

FIGURE 27A

April 5, 1992 00:00

Tm4

J15

```
1  TATCTGCAACCTCTGCGCTACCCAGTGCTCATGAGCGCGCGGGTGTGCCTGCTCATGGT 60 -
   I C N P L R Y P V L M S G R V C L L M V
61  CGTGGCCTCCTGGTGGAGGATCCCTCAACGCCTCCATTCAGACTTCTCTGACCCTTCA 120 -
   V A S W L G G S L N A S I Q T S L T L Q
121 GTTCCCCTACTGTGGATCACGGAAGATCTCCCACTTCTTCTGTGAGGTGCCCTCGCTGCT 180 -
   F P Y C G S R K I S H F F C E V P S L L
181 GAXXXTGGCCTGTGCAGACACTGAAGCCCTATGAGCAGGTACTATTGTGACAGGCGTGGT 240 -
   ? ? A C A D T E A Y E Q V L F V T G V V
```

FIGURE 27B

241	GGTCCTCCTGGTGCCCATACATTCACTTACTGCCTCTTATGCCCCATCCTGGCTGCTGT	300
	V L L V P I T F I T A S Y A L I L A A V	-
301	GCTCCGAATGCACTCTGCGGAGGGAGTCAGAAGGCCCTAGCCACATGCTCCTCTCACCT	360
	L R M H S A E G S Q K A L A T C S S H L	-
361	GACAGTCGTCAATCTTCTATGGGGCCCTTGCTCTACACCTACATGTACCTGCTTCCTA	420
	T V V N L F Y G P L V Y T Y M L P A S Y	-
421	TCACTCACCAGGCCAAGACGACATAGTATCCGCTCTTTTACACCGTTCTCACACCCATGCT	480
	H S P G Q D D I V S V F Y T V L T P M L	-
481	T - 481	
	A	

FIGURE 28

FIGURE 28A

FIGURE 28A

FIGURE 28B

J16

Tm4

1	CATCTGAGGCCCTCTTCACTATCCTACCTCATGCCAGACACCTGTGTGCCAAGATTGC	60	-
	I C R P L H Y P T L M T Q T L C A K I A		
61	CACTGGTGTGCTGGAGGCTTGGCTGGGCCAGTGGTAGAAATTCTCTGGTGCTCG	120	-
	T G C W L G G L A G P V V E I S L V S R		
121	TCTCCTTTTGTGGCCCAATCACATTCACACATCTTTTGTGATTTCCACCTGTGCT	180	-
	L L F C G P N H I Q H I F C D F P P V L		
181	GAGCTTGGCTTGTAATACATCAGTGAATGTCCTGGTAGATTTTATATAAACCTCTG	240	-
	S L A C T D T S V N V L V D F I I N L C		
241	CAAGATCCTGGCCACCTTCCTGCTGATCCTGAGCTCCTACTTGCAGATAATCCGCACAGT	300	-
	K I L A T F L L I L S S Y L Q I I R T V		

FIGURE 28B

```
301 GCTCAAGATTCCCTTCAGCTGCAGGCAAGAAAGCATTCGACTTGTGCTCCCATCT 360 -  
-----+-----+-----+-----+-----+-----+-----+  
L K I P S A A G K K K A F S T C A S H L  
361 CACTGTGGTTCTCATCTTCTATGGGAGCATCCCTTTTCATGTATGTGCGGCTGAAGAAGAC 420 -  
-----+-----+-----+-----+-----+-----+-----+  
T V V L I F Y G S I L F M Y V R L K K S  
421 TTAATCCCTTGACTACGACAGAGCCCTTGGCAGTAGTCTACTCCGTGGTTACCCCTTTCCT 420 -  
-----+-----+-----+-----+-----+-----+-----+  
Y S L D Y D R A L A V V Y S V V T P F L  
G  
481 - 481
```

FIGURE 29

FIGURE 29A

FIGURE 29B

FIGURE 29A

J17

	Tm4	
60 -	AATCTGCAACCCACTGCTTTATTCCACCACAAATGTCCACACAAGTCTGTATCCAGTTGGT -----+-----+-----+-----+-----+	I C N P L L Y S T K M S T Q V C I Q L V
120 -	TGCAGGATCTTATATAGGGGGTTTTCTTAATACTTGCCCTCATCATGTTTACTTTTTCCTC -----+-----+-----+-----+-----+	A G S Y I G G F L N T C L I M F Y F F S
180 -	TTTTCTCTTCTGTGGGCCAATAATAGTTGATCATTTTCTGTGATTTTGCTCCTTTXXXT -----+-----+-----+-----+-----+	F L F C G P N I V D H F F C D F A P ?
240 -	GGAAC TT CGTCTGATGTGAGTGCTCTCTGTAGTTGTTATGTCATTTTCTGCTGGCTC -----+-----+-----+-----+-----+	E L S C S D V S V S V V M S F S A G S
300 -	AGTTACTATGATCACAGTGT TT ATCATAGCCATCT CCTATTCTTACATCCCTCATCACCAT -----+-----+-----+-----+-----+	V T M I T V F I I A I S Y S Y I L I T I

FIGURE 29B

301 CCTGAAGATGTCCTCAACTGAGGGCCGTCACAAGGCTTCTCCACATGTACCTCCACCT 360
-----+-----+-----+-----+-----+
L K M S S T E G R H K A F S T C T S H L -
361 CACTGCAGTCACTCTACTATGGCACCATTACCTTCATTATGTGATGCCCAAGTCCAC 420
-----+-----+-----+-----+-----+
T A V T L Y Y G T I T F I Y V M P K S T -
421 ATACTCTACAGACCAGAACAGGTGGTGTCTGTGTTTACATGGTGGTGATCCCAATGTT 480
-----+-----+-----+-----+-----+
Y S T D Q N K V V S V F Y M V V I P M L -
G
481 - 481

FIGURE 30

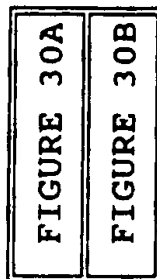


FIGURE 30A

J19

Tm4

1	TATCTGCCACCCTCTGAAGTACACAGTTATCATGAATCACTATTTTGTGTGATGCTGCT	60
	I C H P L K Y T V I M N H Y F C V M L L	-
61	GCTCTTCTGTGTTTCGTTAGCATGTCACATGCGTTGTTCCACATTTTAATGGTGTGAT	120
	L F S V F V S I A H A L F H I L M V L I	-
121	ACTGACTTTCAGCACAAAACCTGAAATCCCTCACTTTTCTGTGAGCTGGCTCATATCAT	180
	L T F S T K T E I P H F F C E L A H I I	-
181	CAAACCTTACCCTGTTCCGATAATTTTATCAAACTATCTGCTGATATACACAGAGTCTGCTT	240
	K L T C S D N F I N Y L L I Y T E S V L	-
241	ATTTTGGTGTTCATATGTAGGATCATTTTGTCTTATATTTACACTGTATCCTCAGT	300
	F F G V H I V G I I I L S Y I Y T V S S V	-

FIGURE 30B

301 TTTAAGAATGTCATTATTGGGAGGAATGTATAAAGCCTTTTCACAATGTGGATCTCATTT 360 -
-----+-----+-----+-----+-----+-----+-----+
L R M S L L G G M Y K A F S T C G S H L
361 GTCGGTTGTCCTCTGTTTATGGCCACAGGTTTGGGGTACACATAAGCTCTCCACTTACTG 420 -
-----+-----+-----+-----+-----+-----+-----+
S V V S V L W H R F W G T H K L S T Y *
421 ACTCTCCAAGGAAGACTGTAGTGGCTTCAGTGATGTACACTGTGGTTACTCAGATGCTG 479 -
-----+-----+-----+-----+-----+-----+-----+
L S K E D C S G F S D V H C G Y S D A

FIGURE 31

FIGURE 31A

FIGURE 31B

FIGURE 31A

J20

[illegible]

FIGURE 31B

181 CCTGTTCTGCACAGATACATCTCTGCTGGAGXXXXXXXXXXXXXXXXXXXXXXXXXXXXX
L F C T D T S L L E ? ? ? ? ? ? ? ? ? ? ? ? ? ? ? ?
240 -

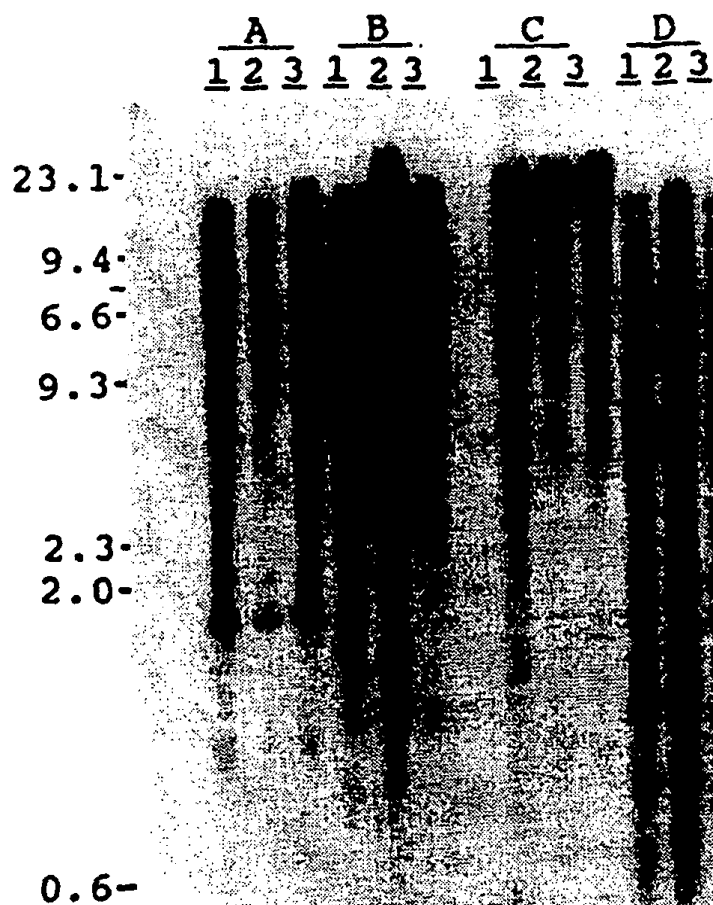
241 XXXXXXXXXXXCCCTTCCTCGATTGTTCTCTCCTACCTTCGCATCCTGGTGGCTGTG
? ? ? ? P F L L I V L S Y L R I L V A V
300

301 ATAAGAAATAGACTCAGCTGAGGGCAGAAAAAGGCCCTTTCAACTTGTGCTTCACACTG
I R I D S A E G R K K A F S T C A S H L
360

361 GCTGTGGTGACCATCTACTATGGAACAGGGCTGATCAGGTACTTGAGGCCCAAGTCCCTT
A V V T I Y Y G T G L I R Y L R P K S L
420

421 TATTCGCTGAGGGAGACAGACTGATCTCTGTGTTCTATGCAGTCATTGGCCCTGCAC TG
Y S A E G D R L I S V F Y A V I G P A L
480

Figur 32



INTERNATIONAL SEARCH REPORT

International application No.
PCT/US92/02741**A. CLASSIFICATION OF SUBJECT MATTER**

IPC(5) : C12N 15/12, 15/63, 15/64, 5/10; C07K 13/00; A01N 33/00; A61K 37/00

US CL : 536/27; 424/418; 435/7.21, 172.3, 240.1, 320.1; 514/2; 530/395

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

U.S. : 536/27; 424/418; 435/7.21, 172.3 240.1, 320.1; 514/2; 530/395

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

CAS ONLINE, MEDLINE, UEMBL, GENBANK, PIR, SWISS PROT, APS

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
<u>X,P</u> <u>Y,P</u>	Molecular Brain Research, Volume 13, No. 1-2, issued March 1992, L. A. Selbie et al., "Novel G protein-coupled receptors: a gene family of putative human olfactory receptor sequences," abstract.	<u>1-32</u> 33-98
<u>Y</u> <u>X</u>	Sensory Syst., Volume 1, No. 1, issued 1987, V. I. Novoselov et al., "The properties of receptor molecules from rat olfactory epithelium," abstract.	<u>1-34, 65-98</u> 35-64
<u>X,P</u> <u>Y,P</u>	Nature, Volume 355, issued 30 January 1992, M. Parmentier et al., "Expression of members of the putative olfactory receptor gene family in mammalian germ cells," pages 453-455, see entire document.	<u>1-32</u> 33-98
<u>Y</u> <u>X</u>	Biochimica Biophysica Acta, Volume 839, No. 3, issued 1985, E. E. Fesenko et al., "Molecular mechanisms of olfactory reception. VI Kinetic characteristics of camphor interaction with binding sites of rat olfactory epithelium," abstract.	<u>1-34, 65-98</u> 35-64

☒ Further documents are listed in the continuation of Box C. ☐ See patent family annex.

- * Special categories of cited documents:
- *A* document defining the general state of the art which is not considered to be part of particular relevance
 - *E* earlier document published on or after the international filing date
 - *L* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
 - *O* document referring to an oral disclosure, use, exhibition or other means
 - *P* document published prior to the international filing date but later than the priority date claimed

Date of the actual completion of the international search

25 June 1992

Date of mailing of the international search report

23 July 1992

Name and mailing address of the ISA/
Commissioner of Patents and Trademarks
Box PCT
Washington, D.C. 20231

Facsimile No. NOT APPLICABLE

Authorized officer

LISA T. BENNETT

Telephone No. (703) 308-3988

INTERNATIONAL SEARCH REPORT

International application No.

PCT/US92/02741

C (Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X,P Y,P	Chemtracts: Organic Chemistry, Volume 4, No. 4, issued 1991, K. Touhara et al., "A novel multigene family may encode odorant receptors: a molecular basis for odor recognition," abstract.	1-32 33-98
Y,P	Chemical Senses, Volume 16, No. 5, issued 1991, R. H. R. Anholt, "Odor recognition and olfactory transduction: the new frontier," abstract.	1-98
Y	Trends in Neuroscience, Volume 14, No. 7, issued 1991, S. Firestein, "A noseful of odor receptors," abstract.	1-98
Y	Proceedings of the National Academy of Sciences, Volume 86, issued November 1989, E. Dancigier et al., "Olfactory marker protein gene: Its structure and olfactory neuron-specific expression in transgenic mice," pages 8565-8569, see entire document.	1-34
Y	Kagaky Kogyo, Volume 40, No. 11, issued 1989, M. Kashiwayanagi et al., "High sensitivity odor sensor using artificial membrane," abstract.	1-98

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1	5	10	15
Ala Ala Leu Val Thr Val Ser Trp Val Thr Gly Val Gly Thr Gly Phe	20	25	30
Leu Pro Ser Leu Leu Ile Ser Lys Leu Asp Phe Cys Gly Pro Asn Arg	35	40	45
Ile Asn His Phe Phe Cys Asp Leu Pro Pro Leu Ile Gln Leu Ser Cys	50	55	60
Ser Ser Val Phe Val Thr Glu Met Ala Ile Phe Val Leu Ser Ile Ala	65	70	75
Val Leu Cys Ile Cys Phe Leu Leu Thr Xaa Xaa Ser Tyr Ile Phe Ile	85	90	95
Val Ser Ser Ile Leu Arg Ile Pro Ser Thr Thr Gly Arg Met Lys Thr	100	105	110
Phe Ser Thr Cys Gly Ser His Leu Ala Val Val Thr Ile Tyr Tyr Gly	115	120	125
Thr Met Ile Ser Met Tyr Val Gly Pro Asn Ala His Leu Ser Pro Glu	130	135	140
Leu Asn Lys Val Ile Ser Val Phe Tyr Thr Val Ile Thr Pro Leu Leu	145	150	155
			160

(2) INFORMATION FOR SEQ ID NO:23:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 646 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

(iii) HYPOTHETICAL: YES

(iv) ANTI-SENSE: NO

(vi) ORIGINAL SOURCE:

- (A) ORGANISM: rat olfactory epithelium
- (B) STRAIN: Sprague-Dawley rat
- (F) TISSUE TYPE: olfactory epithelium

(vii) IMMEDIATE SOURCE:

- (B) CLONE: J11

(ix) FEATURE:

- (A) NAME/KEY: CDS
- (B) LOCATION: 2..646

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:23:

N	GTC	TGC	TTC	TCC	TCC	ACC	ACT	GTC	CCC	AAG	GTA	CTG	GCT	AAC	CAC
Val	Cys	Phe	Ser	Ser	Thr	Val	Pro	Lys	Val	Leu	Ala	Asn	His		
1				5				10							

46

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-72-

ATA CTC AGT AGT CAG GCC ATT TCC TTC TCT GGG TGT CTA ACT CAG CTG Ile Leu Ser Ser Gln Ala Ile Ser Phe Ser Gly Cys Leu Thr Gln Leu 20 25 30	94
TAT TTT CTC TGT GTG TCT GTG AAT ATG GAC AAT TTC CTG CTG GCT GTG Tyr Phe Leu Cys Val Ser Val Asn Met Asp Asn Phe Leu Leu Ala Val 35 40 45	142
ATG GCC TAT GAC AGA TTT GTG GCC ATA TGC CAC CCT TTG TAC TAC ACA Met Ala Tyr Asp Arg Phe Val Ala Ile Cys His Pro Leu Tyr Tyr Thr 50 55 60	190
ACA AAG ATG ACC CAC CAG CTC TGT GTC TTG CTG GTG TCT CGA TCA NNN Thr Lys Met Thr His Gln Leu Cys Val Leu Leu Val Ser Gly Ser Xaa 65 70 75	238
NNN NNN NNN NNN NNN NNN NNN NNN NNN NNN NNN NNN NNN NNN NNN Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa 80 85 90 95	286
NNN NNN NNN NNN NNN NNN NNN NNN NNN NNN NNN NNN NNN NNN NNN Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa 100 105 110	334
NNN NNN NNN NNN NNN NNN NNN NNN NNN NNN NNN NNN NNN NNN NNN Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa 115 120 125	382
NNN NNN NNN NNN NNN NNN NNT GTG ATC ATG GTC ACC CCA TTT GTC TGC Xaa Xaa Xaa Xaa Xaa Xaa Xaa Val Ile Met Val Thr Pro Phe Val Cys 130 135 140	430
ATC CTC ATC TCT TAC ATC TAC ATC ACC AAT GCA GTC CTC AGA GTC TCA Ile Leu Ile Ser Tyr Ile Tyr Ile Thr Asn Ala Val Leu Arg Val Ser 145 150 155	478
TCC TTT AGG GGA GGA TGG AAA GCC TTC TCC ACC TGT GGC TCA CAC CTG Ser Phe Arg Gly Gly Trp Lys Ala Phe Ser Thr Cys Gly Ser His Leu 160 165 170 175	526
GCT GTG GTC TGC CTC TTC TAT GGC ACC ATC ATT GCT GTG TAT TTC AAT Ala Val Val Cys Leu Phe Tyr Gly Thr Ile Ile Ala Val Tyr Phe Asn 180 185 190	574
CCT GTA TCT TCC CAT TCA TCT GAG AAG GAC ACT GCA GCA ACT GTG CTA Pro Val Ser Ser His Ser Ser Glu Lys Asp Thr Ala Ala Thr Val Leu 195 200 205	622
TAC ACA GTG GTG ACT CCC ATG TTG Tyr Thr Val Val Thr Pro Met Leu 210 215	646

(2) INFORMATION FOR SEQ ID NO:24:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 215 amino acids
- (B) TYPE: amino acid
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

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(x1) SEQUENCE DESCRIPTION: SEQ ID NO:24:

```

Val Cys Phe Ser Ser Thr Thr Val Pro Lys Val Leu Ala Asn His Ile
 1           5           10           15
Leu Ser Ser Gln Ala Ile Ser Phe Ser Gly Cys Leu Thr Gln Leu Tyr
          20           25           30
Phe Leu Cys Val Ser Val Asn Met Asp Asn Phe Leu Leu Ala Val Met
          35           40           45
Ala Tyr Asp Arg Phe Val Ala Ile Cys His Pro Leu Tyr Tyr Thr Thr
          50           55           60
Lys Met Thr His Gln Leu Cys Val Leu Leu Val Ser Gly Ser Xaa Xaa
          65           70           75           80
Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa
          85           90           95
Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa
          100          105          110
Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa
          115          120          125
Xaa Xaa Xaa Xaa Xaa Xaa Val Ile Met Val Thr Pro Phe Val Cys Ile
          130          135          140
Leu Ile Ser Tyr Ile Tyr Ile Thr Asn Ala Val Leu Arg Val Ser Ser
          145          150          155          160
Phe Arg Gly Gly Trp Lys Ala Phe Ser Thr Cys Gly Ser His Leu Ala
          165          170          175
Val Val Cys Leu Phe Tyr Gly Thr Ile Ile Ala Val Tyr Phe Asn Pro
          180          185          190
Val Ser Ser His Ser Ser Glu Lys Asp Thr Ala Ala Thr Val Leu Tyr
          195          200          205
Thr Val Val Thr Pro Met Leu
          210          215

```

(2) INFORMATION FOR SEQ ID NO:25:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 646 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA

(iii) HYPOTHETICAL: YES

(iv) ANTI-SENSE: NO

(vi) ORIGINAL SOURCE:

- (A) ORGANISM: rat olfactory epithelium
- (B) STRAIN: Sprague-Dawley rat
- (F) TISSUE TYPE: olfactory epithelium

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-74-

(vii) IMMEDIATE SOURCE:
(B) CLONE: J14

(ix) FEATURE:
(A) NAME/KEY: CDS
(B) LOCATION: 2..646

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:25:

T GTC TGC TTC TCC TCC ACC ACT GTC CCC AAG GTA CTG GCT AAC CAC	46
Val Cys Phe Ser Ser Thr Thr Val Pro Lys Val Leu Ala Asn His	
1 5 10 15	
ATA CTC AGT AGT CAG GCC ATT TCC TTC TCT GGG TGT CTA ACT CAG CTG	94
Ile Leu Ser Ser Gln Ala Ile Ser Phe Ser Gly Cys Leu Thr Gln Leu	
20 25 30	
TAT TTT CTC TGT GTG TCT GTG AAT ATG GAC AAT TTC CTG CTG GCT GTG	142
Tyr Phe Leu Cys Val Ser Val Asn Met Asp Asn Phe Leu Leu Ala Val	
35 40 45	
ATG GCC TAT GAC AGA TTT GTG GCC ATA TGC CAC CCT TTG TAC TAC ACA	190
Met Ala Tyr Asp Arg Phe Val Ala Ile Cys His Pro Leu Tyr Tyr Thr	
50 55 60	
ACA CCG ATG ACC CAC CAG CTC TGT GTC TTG CTG GTC TCT GGA TCA NNN	238
Thr Pro Met Thr His Gln Leu Cys Val Leu Leu Val Ser Gly Ser Xaa	
65 70 75	
NNN NNN NNN NNN NNN NNN NNN NNN NNN NNN NNN NNN NNN NNN NNN	286
Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa	
80 85 90 95	
NNN NNN NNN NNN NNN NNN NNN NNN NNN NNN NNN NNN NNN NNN NNN	334
Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa	
100 105 110	
NNN NNN NNN NNN NNN NNN NNN NNN NNN NNN NNN NNN NNN NNN NNN	382
Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa	
115 120 125	
NNN NNN NNN NNN NNN NNN NNT GTG ATC ATG GTC ACC CCA TTT GTC TGC	430
Xaa Xaa Xaa Xaa Xaa Xaa Xaa Val Ile Met Val Thr Pro Phe Val Cys	
130 135 140	
ATC CTC ATC TCT TAC ATC TAC ATC ACC AAT GCA GTC CTC AGA GTC TCA	478
Ile Leu Ile Ser Tyr Ile Tyr Ile Thr Asn Ala Val Leu Arg Val Ser	
145 150 155	
TCC TTT AGG GGA GGA TGG AAA GCC TTC TCC ACC TGT GGC TCA CAC CTG	526
Ser Phe Arg Gly Gly Trp Lys Ala Phe Ser Thr Cys Gly Ser His Leu	
160 165 170 175	
GCT GTG GTC TGC CTC TTC TAT GGC ACC ATC ATT GCT GTG TAT TTC AAT	574
Ala Val Val Cys Leu Phe Tyr Gly Thr Ile Ile Ala Val Tyr Phe Asn	
180 185 190	
CCT GTA TCT TCC CAT TCA TCT GAG AAG GAC ACT GCA GCA ACT GTG CTA	622
Pro Val Ser Ser His Ser Ser Glu Lys Asp Thr Ala Ala Thr Val Leu	
195 200 205	

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-75-

TAC ACA GTG GTG ACT CCC ATG TTG
 Tyr Thr Val Val Thr Pro Met Leu
 210 215

646

(2) INFORMATION FOR SEQ ID NO:26:

- (1) SEQUENCE CHARACTERISTICS:
 (A) LENGTH: 215 amino acids
 (B) TYPE: amino acid
 (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:26:

Val Cys Phe Ser Ser Thr Thr Val Pro Lys Val Leu Ala Asn His Ile
 1 5 10 15
 Leu Ser Ser Gln Ala Ile Ser Phe Ser Gly Cys Leu Thr Gln Leu Tyr
 20 25 30
 Phe Leu Cys Val Ser Val Asn Met Asp Asn Phe Leu Leu Ala Val Met
 35 40 45
 Ala Tyr Asp Arg Phe Val Ala Ile Cys His Pro Leu Tyr Tyr Thr Thr
 50 55 60
 Pro Met Thr His Gln Leu Cys Val Leu Leu Val Ser Gly Ser Xaa Xaa
 65 70 75 80
 Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa
 85 90 95
 Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa
 100 105 110
 Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa
 115 120 125
 Xaa Xaa Xaa Xaa Xaa Xaa Val Ile Met Val Thr Pro Phe Val Cys Ile
 130 135 140
 Leu Ile Ser Tyr Ile Tyr Ile Thr Asn Ala Val Leu Arg Val Ser Ser
 145 150 155 160
 Phe Arg Gly Gly Trp Lys Ala Phe Ser Thr Cys Gly Ser His Leu Ala
 165 170 175
 Val Val Cys Leu Phe Tyr Gly Thr Ile Ile Ala Val Tyr Phe Asn Pro
 180 185 190
 Val Ser Ser His Ser Ser Glu Lys Asp Thr Ala Ala Thr Val Leu Tyr
 195 200 205
 Thr Val Val Thr Pro Met Leu
 210 215

(2) INFORMATION FOR SEQ ID NO:27:

- (1) SEQUENCE CHARACTERISTICS:

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-76-

(A) LENGTH: 481 base pairs
 (B) TYPE: nucleic acid
 (C) STRANDEDNESS: single
 (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA

(iii) HYPOTHETICAL: YES

(iv) ANTI-SENSE: NO

(vi) ORIGINAL SOURCE:

(A) ORGANISM: rat olfactory epithelium
 (B) STRAIN: Sprague-Dawley rat
 (F) TISSUE TYPE: olfactory epithelium

(vii) IMMEDIATE SOURCE:

(B) CLONE: J15

(ix) FEATURE:

(A) NAME/KEY: CDS
 (B) LOCATION: 2..481

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:27:

T ATC TGC AAC CCT CTG CGC TAC CCA GTG CTC ATG AGC GGC CGG GTG	46
Ile Cys Asn Pro Leu Arg Tyr Pro Val Leu Met Ser Gly Arg Val	
1 5 10 15	
TGC CTG CTC ATG GTC GTG GCC TCC TGG TTG GGA GGA TCC CTC AAC GCC	94
Cys Leu Leu Met Val Val Ala Ser Trp Leu Gly Gly Ser Leu Asn Ala	
20 25 30	
TCC ATT CAG ACT TCT CTG ACC CTT CAG TTC CCC TAC TGT GGA TCA CGG	142
Ser Ile Gln Thr Ser Leu Thr Leu Gln Phe Pro Tyr Cys Gly Ser Arg	
35 40 45	
AAG ATC TCC CAC TTC TTC TGT GAG GTG CCC TCG CTG CTG ANN NTG GCC	190
Lys Ile Ser His Phe Phe Cys Glu Val Pro Ser Leu Leu Xaa Xaa Ala	
50 55 60	
TGT GCA GAC ACT GAA GCC TAT GAG CAG GTA CTA TTT GTG ACA GGC GTG	238
Cys Ala Asp Thr Glu Ala Tyr Glu Gln Val Leu Phe Val Thr Gly Val	
65 70 75	
GTG GTC CTC CTG GTG CCC ATT ACA TTC ATT ACT GCC TCT TAT GCC CTC	286
Val Val Leu Leu Val Pro Ile Thr Phe Ile Thr Ala Ser Tyr Ala Leu	
80 85 90 95	
ATC CTG GCT GCT GTG CTC CGA ATG CAC TCT GCG GAG GGG AGT CAG AAG	334
Ile Leu Ala Ala Val Leu Arg Met His Ser Ala Glu Gly Ser Gln Lys	
100 105 110	
GCC CTA GCC ACA TGC TCC TCT CAC CTG ACA GTC GTC AAT CTC TTC TAT	382
Ala Leu Ala Thr Cys Ser Ser His Leu Thr Val Val Asn Leu Phe Tyr	
115 120 125	
GGG CCC CTT GTC TAC ACC TAC ATG TTA CCT GCT TCC TAT CAC TCA CCA	430
Gly Pro Leu Val Tyr Thr Tyr Met Leu Pro Ala Ser Tyr His Ser Pro	
130 135 140	

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GGC CAA GAC GAC ATA GTA TCC GTC TTT TAC ACC GTT CTC ACA CCC ATG 478
 Gly Gln Asp Asp Ile Val Ser Val Phe Tyr Thr Val Leu Thr Pro Met
 145 150 155

CTT 481
 Leu
 160

(2) INFORMATION FOR SEQ ID NO:28:

- (i) SEQUENCE CHARACTERISTICS:
 (A) LENGTH: 160 amino acids
 (B) TYPE: amino acid
 (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:28:

Ile Cys Asn Pro Leu Arg Tyr Pro Val Leu Met Ser Gly Arg Val Cys
 1 5 10 15
 Leu Leu Met Val Val Ala Ser Trp Leu Gly Gly Ser Leu Asn Ala Ser
 20 25 30
 Ile Gln Thr Ser Leu Thr Leu Gln Phe Pro Tyr Cys Gly Ser Arg Lys
 35 40 45
 Ile Ser His Phe Phe Cys Glu Val Pro Ser Leu Leu Xaa Xaa Ala Cys
 50 55 60
 Ala Asp Thr Glu Ala Tyr Glu Gln Val Leu Phe Val Thr Gly Val Val
 65 70 75 80
 Val Leu Leu Val Pro Ile Thr Phe Ile Thr Ala Ser Tyr Ala Leu Ile
 85 90 95
 Leu Ala Ala Val Leu Arg Met His Ser Ala Glu Gly Ser Gln Lys Ala
 100 105 110
 Leu Ala Thr Cys Ser Ser His Leu Thr Val Val Asn Leu Phe Tyr Gly
 115 120 125
 Pro Leu Val Tyr Thr Tyr Met Leu Pro Ala Ser Tyr His Ser Pro Gly
 130 135 140
 Gln Asp Asp Ile Val Ser Val Phe Tyr Thr Val Leu Thr Pro Met Leu
 145 150 155 160

(2) INFORMATION FOR SEQ ID NO:29:

- (i) SEQUENCE CHARACTERISTICS:
 (A) LENGTH: 481 base pairs
 (B) TYPE: nucleic acid
 (C) STRANDEDNESS: single
 (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA

(iii) HYPOTHETICAL: YES

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(iv) ANTI-SENSE: NO

(vi) ORIGINAL SOURCE:

(A) ORGANISM: rat olfactory epithelium

(B) STRAIN: Sprague-Dawley rat

(F) TISSUE TYPE: olfactory epithelium

(vii) IMMEDIATE SOURCE:

(B) CLONE: J16

(ix) FEATURE:

(A) NAME/KEY: CDS

(B) LOCATION: 2..481

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:29:

C ATC TGT AGG CCT CTT CAC TAT CCT ACC CTC ATG ACC CAG ACA CTG	46
Ile Cys Arg Pro Leu His Tyr Pro Thr Leu Met Thr Gln Thr Leu	
1 5 10 15	
TGT GCC AAG ATT GCC ACT GGT TGC TGG TTG GGA GGC TTG GCT GGG CCA	94
Cys Ala Lys Ile Ala Thr Gly Cys Trp Leu Gly Gly Leu Ala Gly Pro	
20 25 30	
GTG GTA GAA ATT TCC TTG GTG TCT CGT CTC CTT TTT TGT GGC CCC AAT	142
Val Val Glu Ile Ser Leu Val Ser Arg Leu Leu Phe Cys Gly Pro Asn	
35 40 45	
CAC ATT CAA CAC ATC TTT TGT GAT TTC CCA CCT GTG CTG AGC TTG GCT	190
His Ile Gln His Ile Phe Cys Asp Phe Pro Pro Val Leu Ser Leu Ala	
50 55 60	
TGT ACT GAT ACA TCA GTG AAT GTC CTG GTA GAT TTT ATT ATA AAC CTC	238
Cys Thr Asp Thr Ser Val Asn Val Leu Val Asp Phe Ile Ile Asn Leu	
65 70 75	
TGC AAG ATC CTG GCC ACC TTC CTG CTG ATC CTG AGC TCC TAC TTG CAG	286
Cys Lys Ile Leu Ala Thr Phe Leu Leu Ile Leu Ser Ser Tyr Leu Gln	
80 85 90 95	
ATA ATC CGC ACA GTG CTC AAG ATT CCT TCA GCT GCA GGC AAG AAG AAA	334
Ile Ile Arg Thr Val Leu Lys Ile Pro Ser Ala Ala Gly Lys Lys Lys	
100 105 110	
GCA TTC TCG ACT TGT GCC TCC CAT CTC ACT GTG GTT CTC ATC TTC TAT	382
Ala Phe Ser Thr Cys Ala Ser His Leu Thr Val Val Leu Ile Phe Tyr	
115 120 125	
GGG AGC ATC CTT TTC ATG TAT GTG CGG CTG AAG AAG ACT TAC TCC CTT	430
Gly Ser Ile Leu Phe Met Tyr Val Arg Leu Lys Lys Thr Tyr Ser Leu	
130 135 140	
GAC TAC GAC AGA GCC TTG GCA GTA GTC TAC TCC GTG GTT ACC CCT TTC	478
Asp Tyr Asp Arg Ala Leu Ala Val Val Tyr Ser Val Val Thr Pro Phe	
145 150 155	
CTG	481
Leu	
160	

(2) INFORMATION FOR SEQ ID NO:30:

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(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 160 amino acids
- (B) TYPE: amino acid
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:30:

```

Ile Cys Arg Pro Leu His Tyr Pro Thr Leu Met Thr Gln Thr Leu Cys
 1           5           10           15
Ala Lys Ile Ala Thr Gly Cys Trp Leu Gly Gly Leu Ala Gly Pro Val
          20           25           30
Val Glu Ile Ser Leu Val Ser Arg Leu Leu Phe Cys Gly Pro Asn His
          35           40           45
Ile Gln His Ile Phe Cys Asp Phe Pro Pro Val Leu Ser Leu Ala Cys
          50           55           60
Thr Asp Thr Ser Val Asn Val Leu Val Asp Phe Ile Ile Asn Leu Cys
          65           70           75           80
Lys Ile Leu Ala Thr Phe Leu Leu Ile Leu Ser Ser Tyr Leu Gln Ile
          85           90           95
Ile Arg Thr Val Leu Lys Ile Pro Ser Ala Ala Gly Lys Lys Lys Ala
          100          105          110
Phe Ser Thr Cys Ala Ser His Leu Thr Val Val Leu Ile Phe Tyr Gly
          115          120          125
Ser Ile Leu Phe Met Tyr Val Arg Leu Lys Lys Thr Tyr Ser Leu Asp
          130          135          140
Tyr Asp Arg Ala Leu Ala Val Val Tyr Ser Val Val Thr Pro Phe Leu
          145          150          155          160

```

(2) INFORMATION FOR SEQ ID NO:31:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 481 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA

(iii) HYPOTHETICAL: YES

(iv) ANTI-SENSE: NO

(vi) ORIGINAL SOURCE:

- (A) ORGANISM: rat olfactory epithelium
- (B) STRAIN: Sprague-Dawley rat
- (F) TISSUE TYPE: olfactory epithelium

(vii) IMMEDIATE SOURCE:

- (B) CLONE: J17

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(ix) FEATURE:

(A) NAME/KEY: CDS

(B) LOCATION: 2..481

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:31:

A ATC TGC AAC CCA CTG CTT TAT TCC ACC AAA ATG TCC ACA CAA GTC Ile Cys Asn Pro Leu Leu Tyr Ser Thr Lys Met Ser Thr Gln Val 1 5 10 15	46
TGT ATC CAG TTG GTT CCA GGA TCT TAT ATA GGG GGT TTT CTT AAT ACT Cys Ile Gln Leu Val Ala Gly Ser Tyr Ile Gly Gly Phe Leu Asn Thr 20 25 30	94
TGC CTC ATC ATG TTT TAC TTT TTC TCT TTT CTC TTC TGT GGG CCA AAT Cys Leu Ile Met Phe Tyr Phe Phe Ser Phe Leu Phe Cys Gly Pro Asn 35 40 45	142
ATA GTT GAT CAT TTT TTC TGT GAT TTT GCT CCT TTN NTG GAA CTT TCG Ile Val Asp His Phe Phe Cys Asp Phe Ala Pro Xaa Xaa Glu Leu Ser 50 55 60	190
TGC TCT GAT GTG AGT GTC TCT GTA GTT GTT ATG TCA TTT TCT GCT GGC Cys Ser Asp Val Ser Val Ser Val Val Val Met Ser Phe Ser Ala Gly 65 70 75	238
TCA GTT ACT ATG ATC ACA GTG TTT ATC ATA GCC ATC TCC TAT TCT TAC Ser Val Thr Met Ile Thr Val Phe Ile Ile Ala Ile Ser Tyr Ser Tyr 80 85 90 95	286
ATC CTC ATC ACC ATC CTG AAG ATG TCC TCA ACT GAG GGC CGT CAC AAG Ile Leu Ile Thr Ile Leu Lys Met Ser Ser Thr Glu Gly Arg His Lys 100 105 110	334
GCT TTC TCC ACA TGT ACC TCC CAC CTC ACT GCA GTC ACT CTC TAC TAT Ala Phe Ser Thr Cys Thr Ser His Leu Thr Ala Val Thr Leu Tyr Tyr 115 120 125	382
GGC ACC ATT ACC TTC ATT TAT GTG ATG CCC AAG TCC ACA TAC TCT ACA Gly Thr Ile Thr Phe Ile Tyr Val Met Pro Lys Ser Thr Tyr Ser Thr 130 135 140	430
GAC CAG AAC AAG GTG GTG TCT GTG TTT TAC ATG GTG GTG ATC CCA ATG Asp Gln Asn Lys Val Val Ser Val Phe Tyr Met Val Val Ile Pro Met 145 150 155	478
TTG Leu 160	481

(2) INFORMATION FOR SEQ ID NO:32:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 160 amino acids
- (B) TYPE: amino acid
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:32:

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```

Ile Cys Asn Pro Leu Leu Tyr Ser Thr Lys Met Ser Thr Gln Val Cys
 1           5           10           15
Ile Gln Leu Val Ala Gly Ser Tyr Ile Gly Gly Phe Leu Asn Thr Cys
           20           25           30
Leu Ile Met Phe Tyr Phe Phe Ser Phe Leu Phe Cys Gly Pro Asn Ile
           35           40           45
Val Asp His Phe Phe Cys Asp Phe Ala Pro Xaa Xaa Glu Leu Ser Cys
           50           55           60
Ser Asp Val Ser Val Ser Val Val Val Met Ser Phe Ser Ala Gly Ser
           65           70           75           80
Val Thr Met Ile Thr Val Phe Ile Ile Ala Ile Ser Tyr Ser Tyr Ile
           85           90           95
Leu Ile Thr Ile Leu Lys Met Ser Ser Thr Glu Gly Arg His Lys Ala
           100           105           110
Phe Ser Thr Cys Thr Ser His Leu Thr Ala Val Thr Leu Tyr Tyr Gly
           115           120           125
Thr Ile Thr Phe Ile Tyr Val Met Pro Lys Ser Thr Tyr Ser Thr Asp
           130           135           140
Gln Asn Lys Val Val Ser Val Phe Tyr Met Val Val Ile Pro Met Leu
           145           150           155           160

```

(2) INFORMATION FOR SEQ ID NO:33:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 479 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA

(iii) HYPOTHETICAL: YES

(iv) ANTI-SENSE: NO

(vi) ORIGINAL SOURCE:

- (A) ORGANISM: rat olfactory epithelium
- (B) STRAIN: Sprague-Dawley rat
- (F) TISSUE TYPE: olfactory epithelium

(vii) IMMEDIATE SOURCE:

- (B) CLONE: J19

(ix) FEATURE:

- (A) NAME/KEY: CDS
- (B) LOCATION: 2..479

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:33:

```

T ATC TGC CAC CCT CTG AAG TAC ACA GTT ATC ATG AAT CAC TAT TTT
Ile Cys His Pro Leu Lys Tyr Thr Val Ile Met Asn His Tyr Phe

```

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1	5	10	15	
TGT GTG ATG CTG CTG CTC TTC TCT GTG TTC GTT AGC ATT GCA CAT GCG				94
Cys Val Met Leu Leu Leu Phe Ser Val Phe Val Ser Ile Ala His Ala	20	25	30	
TTG TTC CAC ATT TTA ATG GTG TTG ATA CTG ACT TTC AGC ACA AAA ACT				142
Leu Phe His Ile Leu Met Val Leu Ile Leu Thr Phe Ser Thr Lys Thr	35	40	45	
GAA ATC CCT CAC TTT TTC TGT GAG CTG GCT CAT ATC ATC AAA CTT ACC				190
Glu Ile Pro His Phe Phe Cys Glu Leu Ala His Ile Ile Lys Leu Thr	50	55	60	
TGT TCC GAT AAT TTT ATC AAC TAT CTG CTG ATA TAC ACA GAG TCT GTC				238
Cys Ser Asp Asn Phe Ile Asn Tyr Leu Leu Ile Tyr Thr Glu Ser Val	65	70	75	
TTA TTT TTT GGT GTT CAT ATT GTA GGG ATC ATT TTG TCT TAT ATT TAC				286
Leu Phe Phe Gly Val His Ile Val Gly Ile Ile Leu Ser Tyr Ile Tyr	80	85	90	95
ACT GTA TCC TCA GTT TTA AGA ATG TCA TTA TTG GGA GGA ATG TAT AAA				334
Thr Val Ser Ser Val Leu Arg Met Ser Leu Leu Gly Gly Met Tyr Lys	100	105	110	
GCC TTT TCA ACA TGT GGA TCT CAT TTG TCG GTT GTC TCT GTT TTA TGG				382
Ala Phe Ser Thr Cys Gly Ser His Leu Ser Val Val Ser Val Leu Trp	115	120	125	
CAC AGG TTT TGG GGT ACA CAT AAG CTC TCC ACT TAC TGA CTC TCC AAG				430
His Arg Phe Trp Gly Thr His Lys Leu Ser Thr Tyr * Leu Ser Lys	130	135	140	
GAA GAC TGT AGT GGC TTC AGT GAT GTA CAC TGT GGT TAC TCA GAT GCT G				479
Glu Asp Cys Ser Gly Phe Ser Asp Val His Cys Gly Tyr Ser Asp Ala	145	150	155	

(2) INFORMATION FOR SEQ ID NO:34:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 159 amino acids
- (B) TYPE: amino acid
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:34:

Ile Cys His Pro Leu Lys Tyr Thr Val Ile Met Asn His Tyr Phe Cys
 1 5 10 15
 Val Met Leu Leu Leu Phe Ser Val Phe Val Ser Ile Ala His Ala Leu
 20 25 30
 Phe His Ile Leu Met Val Leu Ile Leu Thr Phe Ser Thr Lys Thr Glu
 35 40 45
 Ile Pro His Phe Phe Cys Glu Leu Ala His Ile Ile Lys Leu Thr Cys
 50 55 60

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```

Ser Asp Asn Phe Ile Asn Tyr Leu Leu Ile Tyr Thr lu Ser val Leu
65              70              75              80
Phe Phe Gly Val His Ile Val Gly Ile Ile Leu Ser Tyr Ile Tyr Thr
85              90              95
Val Ser Ser Val Leu Arg Met Ser Leu Leu Gly Gly Met Tyr Lys Ala
100            105            110
Phe Ser Thr Cys Gly Ser His Leu Ser Val Val Ser Val Leu Trp His
115            120            125
Arg Phe Trp Gly Thr His Lys Leu Ser Thr Tyr * Leu Ser Lys Glu
130            135            140
Asp Cys Ser Gly Phe Ser Asp Val His Cys Gly Tyr Ser Asp Ala
145            150            155

```

(2) INFORMATION FOR SEQ ID NO:35:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 481 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA

(iii) HYPOTHETICAL: YES

(iv) ANTI-SENSE: NO

(vi) ORIGINAL SOURCE:

- (A) ORGANISM: rat olfactory epithelium
- (B) STRAIN: Sprague-Dawley rat
- (F) TISSUE TYPE: olfactory epithelium

(vii) IMMEDIATE SOURCE:

- (B) CLONE: J20

(ix) FEATURE:

- (A) NAME/KEY: CDS
- (B) LOCATION: 2..481

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:35:

```

A ATC TGC TAC CCA CTG AGG TAC CTT CTC ATC ATG AGC TGG GTG GTG      46
  Ile Cys Tyr Pro Leu Arg Tyr Leu Leu Ile Met Ser Trp Val Val
    1              5              10              15

TGC ACA GCA CTG TCC GTG GCA ATC TGG GTC ATA GGC TTT TGT GCC TCC      94
  Cys Thr Ala Leu Ser Val Ala Ile Trp Val Ile Gly Phe Cys Ala Ser
    20              25              30

GTT ATA CCT CTC TGC TTC ACG ATC CTC CCA CTC TGT GGT CCT TAC GTC      142
  Val Ile Pro Leu Cys Phe Thr Ile Leu Pro Leu Cys Gly Pro Tyr Val
    35              40              45

GTT GAT TAT CTT TTC TGC GAG CTG CCC ATC CTT CTG CAC CTG TTC TGC      190
  Val Asp Tyr Leu Phe Cys Glu Leu Pro Ile Leu Leu His Leu Phe Cys
    50              55              60

ACA GAT ACA TCT CTC CTG GAG NNN NNN NNN NNN NNN NNN NNN NNN      238
  Thr Asp Thr Ser Leu Leu Glu Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa
    65              70              75

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NNN NNN NNN NNN NNN CCC TTC CTC CTG ATT GTT CTC TCC TAC CTT CGC Xaa Xaa Xaa Xaa Xaa Pro Phe Leu Leu Ile Val Leu Ser Tyr Leu Arg 80 85 90 95	286
ATC CTG GTG GCT GTG ATA AGA ATA GAC TCA GCT GAG GGC AGA AAA AAG Ile Leu Val Ala Val Ile Arg Ile Asp Ser Ala Glu Gly Arg Lys Lys 100 105 110	334
GCC TTT TCA ACT TGT GCT TCA CAC TTG GCT GTG GTG ACC ATC TAC TAT Ala Phe Ser Thr Cys Ala Ser His Leu Ala Val Val Thr Ile Tyr Tyr 115 120 125	382
GGA ACA GGG CTG ATC AGG TAC TTG AGG CCC AAG TCC CTT TAT TCC GCT Gly Thr Gly Leu Ile Arg Tyr Leu Arg Pro Lys Ser Leu Tyr Ser Ala 130 135 140	430
GAG GGA GAC AGA CTG ATC TCT GTG TTC TAT GCA GTC ATT GGC CCT GCA Glu Gly Asp Arg Leu Ile Ser Val Phe Tyr Ala Val Ile Gly Pro Ala 145 150 155	478
CTG Leu 160	481

(2) INFORMATION FOR SEQ ID NO:36:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 160 amino acids
- (B) TYPE: amino acid
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:36:

Ile Cys Tyr Pro Leu Arg Tyr Leu Leu Ile Met Ser Trp Val Val Cys 1 5 10 15
Thr Ala Leu Ser Val Ala Ile Trp Val Ile Gly Phe Cys Ala Ser Val 20 25 30
Ile Pro Leu Cys Phe Thr Ile Leu Pro Leu Cys Gly Pro Tyr Val Val 35 40 45
Asp Tyr Leu Phe Cys Glu Leu Pro Ile Leu Leu His Leu Phe Cys Thr 50 55 60
Asp Thr Ser Leu Leu Glu Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa 65 70 75 80
Xaa Xaa Xaa Xaa Pro Phe Leu Leu Ile Val Leu Ser Tyr Leu Arg Ile 85 90 95
Leu Val Ala Val Ile Arg Ile Asp Ser Ala Glu Gly Arg Lys Lys Ala 100 105 110
Phe Ser Thr Cys Ala Ser His Leu Ala Val Val Thr Ile Tyr Tyr Gly 115 120 125
Thr Gly Leu Ile Arg Tyr Leu Arg Pro Lys Ser Leu Tyr Ser Ala Glu 130 135 140
Gly Asp Arg Leu Ile Ser Val Phe Tyr Ala Val Ile Gly Pro Ala Leu 145 150 155 160

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What is claimed is:

1. An isolated nucleic acid molecule encoding an odorant receptor.
2. An isolated DNA of claim 1.
3. An isolated cDNA of claim 2.
4. An isolated cDNA of claim 3 wherein the sequence of the cDNA has the nucleotide sequence shown in Figure 9.
5. An isolated cDNA of claim 3 wherein the sequence of the cDNA has the nucleotide sequence shown in Figure 10.
6. An isolated cDNA of claim 3 wherein the sequence of the cDNA has the nucleotide sequence shown in Figure 11.
7. An isolated cDNA of claim 3 wherein the sequence of the cDNA has the nucleotide sequence shown in Figure 12.
8. An isolated cDNA of claim 3 wherein the sequence of the cDNA has the nucleotide sequence shown in Figure 13.
9. An isolated cDNA of claim 3 wherein the sequence of the cDNA has the nucleotide sequence shown in Figure 14.
10. An isolated cDNA of claim 3 wherein the sequence of the cDNA has the nucleotide sequence shown in Figure 15.
11. An isolated cDNA of claim 3 wherein the sequence of the cDNA has the nucleotide sequence shown in Figure 16.
12. An isolated cDNA of claim 3 wherein the sequence of the cDNA has the nucleotide sequenc shown in Figure 17.

13. An isolated cDNA of claim 3 wherein the sequence of the cDNA has the nucleotide sequence shown in Figure 18.
- 5 14. An isolated cDNA of claim 3 wherein the sequence of the cDNA has the nucleotide sequence shown in Figure 19.
- 15 15. An isolated cDNA of claim 3 wherein the sequence of the cDNA has the nucleotide sequence shown in Figure 20.
- 10 16. An isolated cDNA of claim 3 wherein the sequence of the cDNA has the nucleotide sequence shown in Figure 21.
- 15 17. An isolated cDNA of claim 3 wherein the sequence of the cDNA has the nucleotide sequence shown in Figure 22.
18. An isolated cDNA of claim 3 wherein the sequence of the cDNA has the nucleotide sequence shown in Figure 23.
- 20 19. An isolated cDNA of claim 3 wherein the sequence of the cDNA has the nucleotide sequence shown in Figure 24.
20. An isolated cDNA of claim 3 wherein the sequence of the cDNA has the nucleotide sequence shown in Figure 25.
- 25 21. An isolated cDNA of claim 3 wherein the sequence of the cDNA has the nucleotide sequence shown in Figure 26.
22. An isolated cDNA of claim 3 wherein the sequence of the cDNA has the nucleotide sequence shown in Figure 27.
- 30 23. An isolated cDNA of claim 3 wherein the sequence of the cDNA has the nucleotide sequence shown in Figure 28.
- 35 24. An isolated cDNA of claim 3 wherein the sequence of the cDNA has the nucleotide sequence shown in Figure 29.

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25. An isolated cDNA of claim 3 wherein the sequence of the cDNA has the nucleotide sequence shown in Figure 30.
- 5 26. An isolated cDNA of claim 3 wherein the sequence of the cDNA has the nucleotide sequence shown in Figure 31.
27. An isolated cDNA of claim 3 encoding an insect odorant receptor.
- 10 28. An isolated cDNA of claim 3 encoding a vertebrate odorant receptor.
29. An isolated cDNA of claim 3 encoding a fish odorant receptor.
- 15 30. An isolated cDNA of claim 3 encoding a mammalian odorant receptor.
31. An isolated cDNA of claim 30 wherein the mammalian odorant receptor is a human odorant receptor.
- 20 32. An isolated cDNA of claim 30 wherein the mammalian odorant receptor is a rat, dog or mouse odorant receptor.
- 25 33. An expression vector comprising the cDNA of claim 3 and the sequence elements necessary for replication and expression in a suitable host.
- 30 34. An expression vector comprising the cDNA of any of claims 4-19 and the sequence elements necessary for replication and expression in a suitable host.
- 35 35. A purified protein encoding an odorant receptor.

36. A purified protein of claim 35 wherein the amino acid sequence is the sequence in Figure 9.
37. A purified protein of claim 35 wherein the amino acid sequence is the sequence in Figure 10.
38. A purified protein of claim 35 wherein the amino acid sequence is the sequence in Figure 11.
39. A purified protein of claim 35 wherein the amino acid sequence is the sequence in Figure 12.
40. A purified protein of claim 35 wherein the amino acid sequence is the sequence in Figure 13.
41. A purified protein of claim 35 wherein the amino acid sequence is the sequence in Figure 14.
42. A purified protein of claim 35 wherein the amino acid sequence is the sequence in Figure 15.
43. A purified protein of claim 35 wherein the amino acid sequence is the sequence in Figure 16.
44. A purified protein of claim 35 wherein the amino acid sequence is the sequence in Figure 17.
45. A purified protein of claim 35 wherein the amino acid sequence is the sequence in Figure 18.
46. A purified protein of claim 35 wherein the amino acid sequence is the sequence in Figure 19.
47. A purified protein of claim 35 wherein the amino acid sequence is the sequence in Figure 20.

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48. A purified protein of claim 35 wherein the amino acid sequence is the sequence in Figure 21.
49. A purified protein of claim 35 wherein the amino acid sequence is the sequence in Figure 22.
50. A purified protein of claim 35 wherein the amino acid sequence is the sequence in Figure 23.
51. A purified protein of claim 35 wherein the amino acid sequence is the sequence in Figure 24.
52. A purified protein of claim 35 wherein the amino acid sequence is the sequence in Figure 25.
53. A purified protein of claim 35 wherein the amino acid sequence is the sequence in Figure 26.
54. A purified protein of claim 35 wherein the amino acid sequence is the sequence in Figure 27.
55. A purified protein of claim 35 wherein the amino acid sequence is the sequence in Figure 28.
56. A purified protein of claim 35 wherein the amino acid sequence is the sequence in Figure 29.
57. A purified protein of claim 35 wherein the amino acid sequence is the sequence in Figure 31.
58. A purified protein of claim 35 encoding an insect odorant receptor.
59. A purified protein of claim 35 encoding a vertebrate odorant receptor.

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60. A purified protein of claim 35 encoding a fish odorant receptor.
- 5 61. A purified protein of claim 35 encoding a mammalian odorant receptor.
62. A purified protein of claim 61 wherein the mammalian odorant receptor is a human odorant receptor.
- 10 63. A purified protein of claim 61 wherein the mammalian odorant receptor is a rat, dog or mouse odorant receptor.
- 15 64. A purified protein of claim 35 which has 7 transmembrane regions and whose third cytoplasmic loop from the N-terminus is approximately 17 amino acid long.
- 20 65. A method of transforming cells which comprises transfecting a host cell with a suitable expression vector of claim 33.
- 25 66. A method of transforming cells which comprises transfecting a host cell with a suitable expression vector of claim 34.
67. Cells transformed by the method of claim 65.
- 30 68. Transformed cells of claim 67 wherein the cells are olfactory cells.
69. Transformed cells of claim 67 wherein the cells are non-olfactory cells.
- 35

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70. A method of identifying a desired odorant ligand comprising contacting transformed non-olfactory cells of claim 69, expressing a known odorant receptor with a series of odorant ligands and determining which ligands bind to the receptors present on the non-olfactory cells.
71. A method of identifying a desired odorant receptor comprising contacting a series of transformed non-olfactory cells of claim 69 with a known odorant ligand and determining which odorant receptor binds with the odorant ligand.
72. A method of detecting an odor which comprises:
- a) identifying a odorant receptor which binds the desired odorant ligand by the method of claim 71 and;
 - b) imbedding the receptor in a membrane such that when the odorant ligand binds with the receptor identified in a) above, a detectable signal is produced.
73. A method of claim 72 wherein the desired odorant is a pheromone.
74. A method of claim 72 wherein the desired odorant ligand is the vapors emanating from cocaine, marijuana, heroin, hashish, or angel dust.
75. A method of claim 72 wherein the desired odorant ligand is the vapors emanating from gasoline, natural gas or alcohol.

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76. A method of claim 72 wherein the desired odorant ligand is the vapors emanating from decayed human flesh.
- 5 77. A method of claim 72 wherein the desired odorant ligand is the vapors emanating from explosives, plastic explosives, firearms, or gun powder.
78. A method of claim 72 wherein the desired odorant ligand is toxic fumes, noxious fumes or dangerous fumes.
- 10 79. A method of claim 72 wherein the membrane is a cell membrane.
80. A method of claim 72 wherein the membrane is an olfactory cell membrane.
- 15 81. A method of claim 72 wherein the membrane is a synthetic membrane.
- 20 82. A method of claim 72 wherein the detectable signal is a color change, phosphorescence, or radioactivity.
83. A method of quantifying the amount of an odorant ligand present in a sample which comprises the method of claim 72 wherein the detectable signal is quantified.
- 25 84. A method of developing fragrances which comprises identifying a desired odorant receptor by the method of claim 71 then contacting non-olfactory cells, which have been transfected with an expression vector containing the cDNA of the desired odorant receptor such that the receptor is expressed upon the surface of the non-olfactory cell, with a series of compounds to determine which ones bind with the receptor.
- 30
- 35

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- 5 85. A method of identifying an odorant fingerprint which comprises contacting a series of cells, which have been transformed such that each express a known odorant receptor, with a desired sample and determining the type and quantity of the odorant ligands present in the sample.
- 10 86. A method of identifying odorant ligands which inhibit the activity of a desired odorant receptor which comprises contacting the desired odorant receptor with a series of compounds and determining which compounds inhibit the odorant ligand - odorant receptor interaction.
- 15 87. A method of identifying appetite suppressant compounds which comprises identifying odorant ligands by the method of claim 86 wherein the desired odorant receptor is that which is associated with the perception of food.
- 20 88. A method of controlling appetite in a subject which comprises contacting the olfactory epithelium of the subject with the odorant ligands identified by the method of claim 87.
- 25 89. A nasal spray, to control appetite comprising the compounds identified by the method of claim 87 in a suitable carrier.
- 30 90. A method of trapping odors which comprises contacting a membrane which contains multiples of the desired odorant receptor, with a sample such that the desired odorant ligand is absorbed by the binding of the odorant ligand to the odorant receptor.
- 35

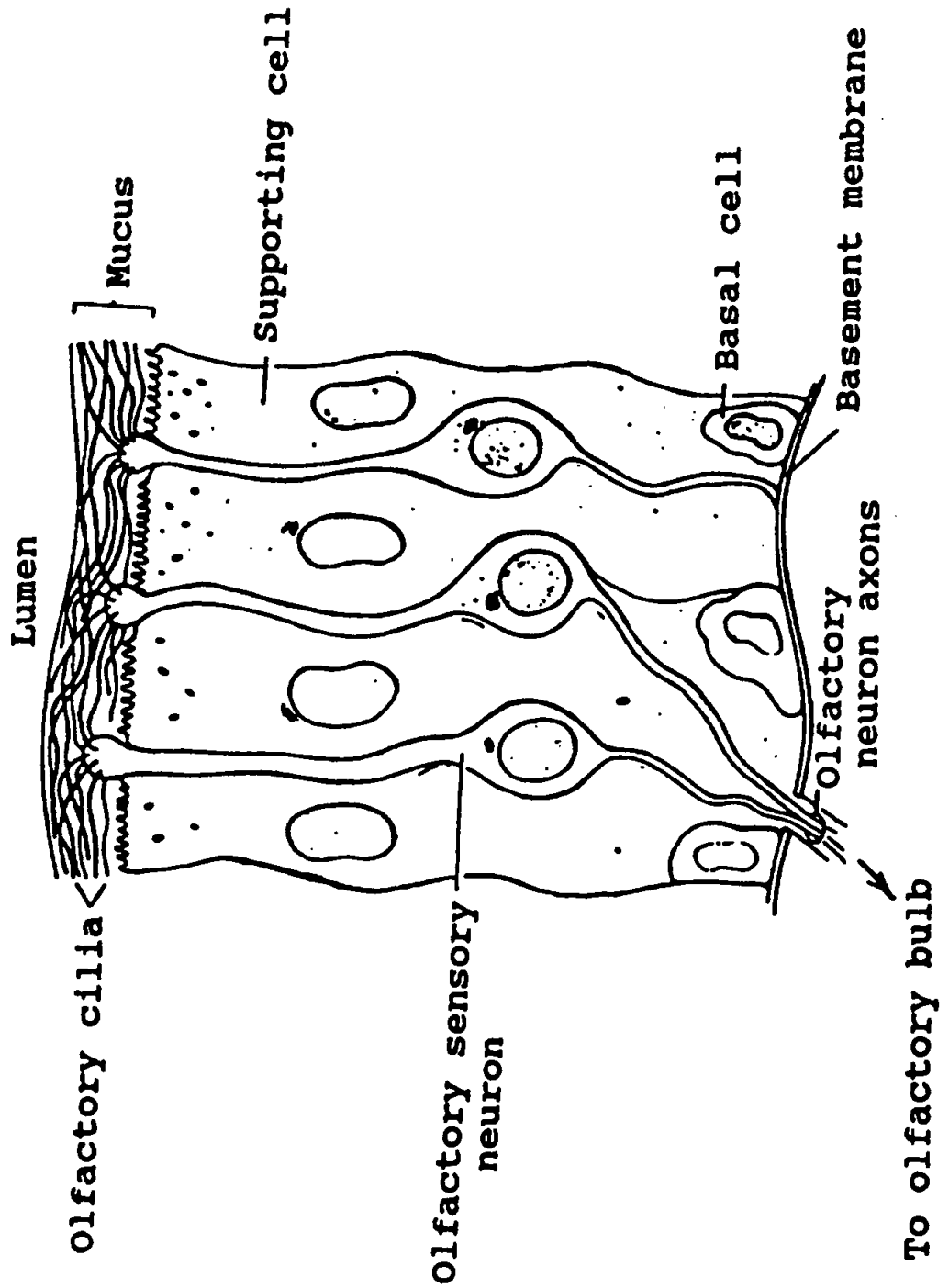
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91. An odor trap employing the method of claim 90.
- 5 92. A method of controlling pest populations which comprises identifying odorant ligands by the method of claim 70 which are alarm odorant ligands and spraying the desired area with the identified odorant ligands.
- 10 93. A method of controlling a pest population which comprises identifying odorant ligands by the method of claim 70 which interfere with the interaction between the odorant ligands and the odorant receptors which are associated with fertility.
- 15 94. A method of claim 92 or 93 wherein the pest population is a population of insects.
95. A method of claim 92 or 93 wherein the pest population is a population of rodents.
- 20 96. A method of claim 95 wherein the population of rodents is a population of mice or rats.
- 25 97. A method of promoting fertility which comprises employing the method of claim 70 to identify odorant ligands which interact with the odorant receptors associated with fertility and administering the identified odorant ligands to a subject.
- 30 98. A method of inhibiting fertility which comprises employing the method of claim 70 to identifying odorant ligands which inhibit the interaction between the odorant ligands and the odorant receptors associated with fertility and administering the identified odorant ligands to a subject.

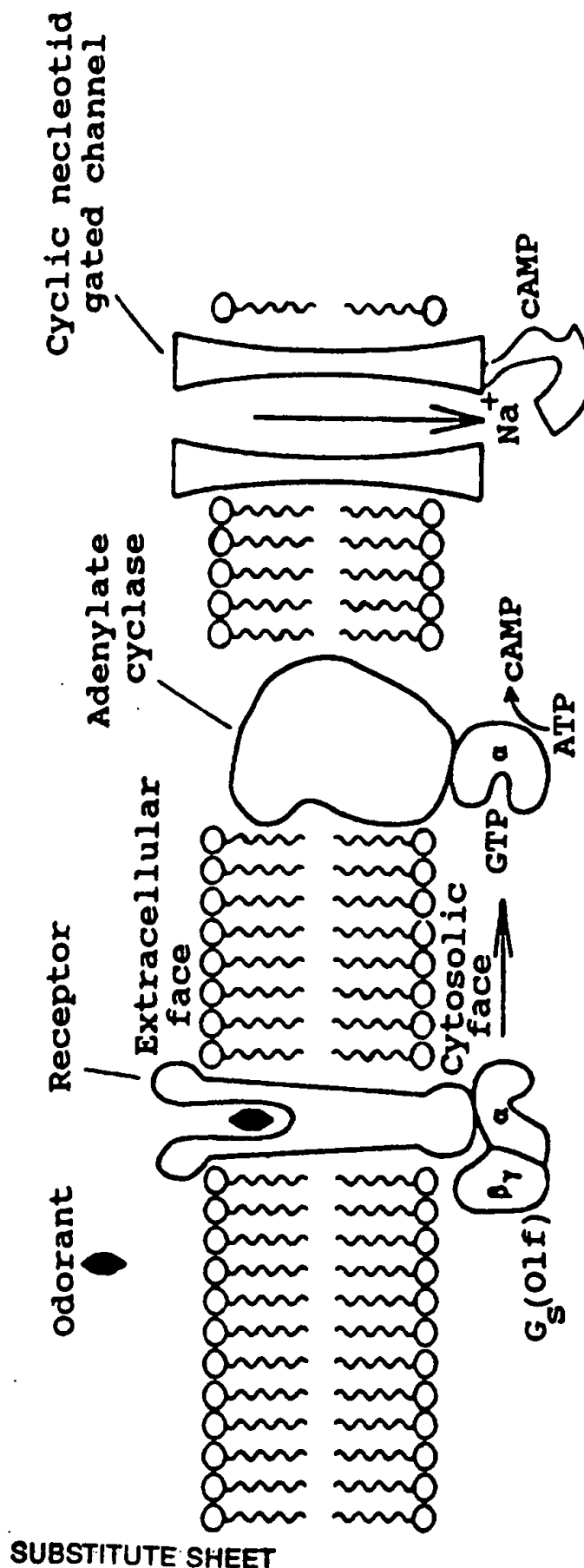
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Figure 1A

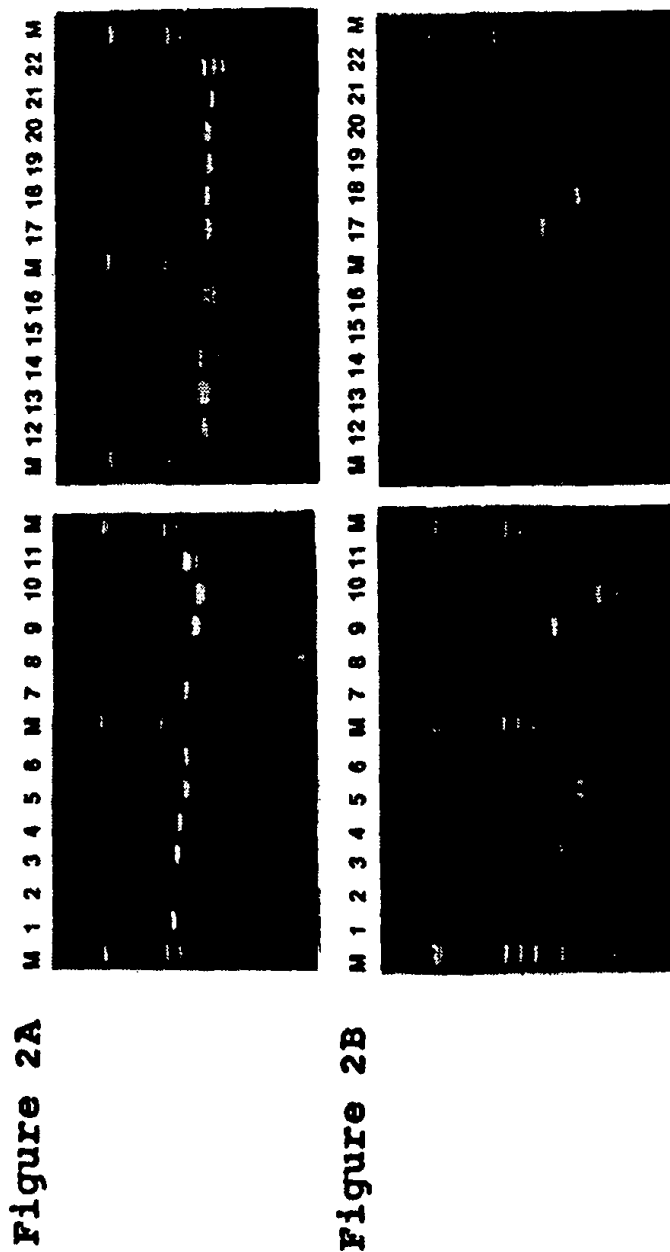


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Figure 1B

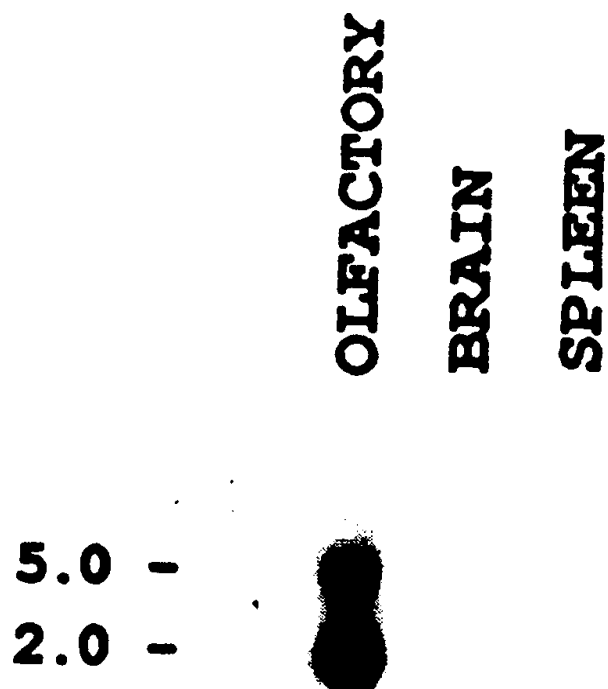


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Figur 3



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Figur 4A

F3				M	D	S	S	N	R	T	R	V	S	E	11
F5				M	S	S	T	N	Q	S	S	V	T	E	11
F6	N	A	W	S	T	G	Q	N	L	S	T	P	G	P	14
F12				M	E	S	G	N	S	T	R	R	F	S	12
I3				M	N	-	-	N	Q	T	F	I	T	Q	9
I7				M	E	R	R	N	H	S	G	R	V	S	12
I8				M	N	-	-	N	K	T	V	I	T	H	9
I8				M	T	R	R	N	Q	T	A	I	S	Q	11
I14				M	T	G	N	N	Q	T	L	I	L	E	11
I15				M	T	E	E	N	Q	T	V	I	S	Q	11

F3	F	L	L	L	G	F	V	E	N	K	D	L	Q	P	25
F5	F	L	L	L	G	L	S	R	Q	P	Q	Q	Q	Q	25
F6	F	I	L	L	G	F	P	G	P	R	S	M	R	I	28
F12	F	F	L	L	G	F	T	E	N	P	Q	L	H	F	26
I3	F	L	L	L	G	L	P	I	P	E	E	H	Q	H	23
I7	F	V	L	L	G	F	P	A	P	A	P	L	R	V	26
I8	F	L	L	L	G	L	P	I	P	P	E	H	Q	Q	23
I9	F	F	L	L	G	L	P	F	P	P	E	Y	Q	H	25
I14	F	L	L	L	G	L	P	I	P	S	E	Y	H	L	25
I15	F	L	L	L	F	L	P	I	P	S	E	H	Q	H	25

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Figur 4B

	<u>I</u>	
F3	L I Y G L F L S N Y L V T V	39
F5	L L F L L F L I N Y L A T V	39
F6	G L F L L F L V N Y L L T V	42
F12	L I F A L F L S N Y L V T V	40
I3	L F Y A L F L V N Y L T T I	37
I7	L L F F L S L L X Y V L V L	40
I8	L F F A L F L I N Y L T T F	37
I9	L F Y A L F L A N Y L T T L	39
I14	L F Y A L F L A N Y L T I I	29
I15	V F Y A L F L S N Y L T T V	39

	<u>I</u>	
F3	I G N I S I I V A I I S D P	53
F5	L G N L L I I L A I G T D S	53
F6	V G N L A I I S L V G A H R	56
F12	L G N L L I I M A I I T Q S	54
I3	L G N L L I I V L V Q L D S	51
I7	T E N M L I I I A I R N H P	54
I8	L G N L L I V V L V Q L D S	51
I9	L G N L I I I I L I L L D S	53
I14	L G N L L I I V L V R L D S	53
I15	L G N L I I I I L I H L D S	53

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Figur 4C

II

F3	C L H T P N Y F F L S N L S	67
F5	R L H T P N Y F F L S N L S	67
F6	C L Q T P N Y F F L C N L S	70
F12	H L H T P N Y F F L A N L S	68
I3	Q L H T P N Y L F L S N L S	65
I7	T L H K P N Y F F L A N M S	68
I8	H L H T P N Y L F L S N L S	65
I9	H L H T P N Y L F L S N L S	67
I14	H L H M P N Y L F L S N L S	67
I15	H L H T P N Y L F L S N L S	67

II

F3	F V D I C F I S T T V P K M	81
F5	F V D V C F S S T T V P K V	81
F6	F L E I W F T T A C V P K T	84
F12	F V D I C F T S T T I P K M	82
I3	F S D L C F S S V T M P K L	79
I7	F L E I W Y V T V T I P K M	82
I8	F S D L C F S S V T M L K L	79
I9	F A D L C F S S V T M P K L	67
I14	F S D L C F S S V T M P K L	67
I15	F S D L C F S S V T M P K L	67

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Figur 4D

F3	L	-	-	-	-	V	N	I	Q	T	Q	N	N	V	91
F5	L	-	-	-	-	A	N	H	I	L	G	S	Q	A	91
F6	L	-	-	-	-	A	T	F	A	P	R	G	G	V	94
F12	L	-	-	-	-	V	N	I	Y	T	Q	S	K	S	92
I3	L	-	-	-	-	Q	N	M	R	S	Q	K	T	S	89
I7	L	A	G	F	I	G	S	K	E	N	H	G	Q	L	96
I8	L	-	-	-	-	Q	N	I	Q	S	Q	V	P	S	89
I9	L	-	-	-	-	Q	N	M	Q	S	Q	V	P	S	91
I14	L	-	-	-	-	Q	N	M	Q	S	Q	V	P	S	91
I15	L	-	-	-	-	Q	N	M	Q	S	Q	V	P	S	91

	III														
F3	I	T	Y	A	G	C	I	T	Q	I	Y	F	F	L	105
F5	I	S	F	S	G	C	L	T	Q	L	Y	F	L	A	105
F6	I	S	L	A	G	C	A	T	Q	M	Y	F	V	F	108
F12	I	T	Y	E	D	C	I	S	Q	M	C	V	F	L	106
I3	I	P	Y	G	G	C	L	A	Q	T	Y	F	F	M	103
I7	I	S	F	E	A	C	M	T	Q	L	Y	F	F	L	110
I8	I	S	Y	A	G	C	L	T	Q	I	F	F	F	L	103
I9	I	P	Y	A	G	C	L	A	Q	I	Y	F	F	L	105
I14	I	S	Y	T	G	C	L	T	Q	L	Y	F	F	M	105
I15	I	P	F	A	G	C	L	T	Q	L	Y	F	Y	L	105

Figur 4E

	<u>III</u>	
F3	L F V E L D N F L L T I M A	119
F5	V F G N M D N F L L A V M S	119
F6	S L G C T E Y F L L A V M A	122
F12	V F A I L G N F L L A V M A	120
I3	V F G D M E S F L L V A M A	117
I7	G L G C T E C V L L A V M A	124
I8	L F G Y L G N F L L V A M A	117
I9	F F G D L G N F L L V A M A	119
I14	V F G D M E S F L L V V M A	119
I15	Y F A D L E S F L L V A M A	119

	<u>III</u>	
F3	Y D R Y V A I C H P M H Y T	133
F5	Y D R F V A I C H P L H Y T	133
F6	Y D R Y L A I C L P L R Y G	136
F12	Y D R Y V A X C H P L C Y T	134
I3	Y D R Y V A I C F P L H Y T	131
I7	Y D R Y V A I C H P L H Y P	138
I8	Y D R Y V A I C F P L H Y T	131
I9	Y D R Y V A I C F P L H Y M	133
I14	Y D R Y V A I C F P L R Y T	133
I15	Y D R Y V A I C F P L H Y M	133

Figure 4F

	<u>IV</u>														
F3	V	I	N	N	Y	K	L	C	G	F	L	V	L	V	147
F5	T	K	N	T	R	Q	L	C	V	L	L	V	V	G	147
F6	G	I	N	T	P	G	L	A	M	R	L	A	L	G	150
F12	V	I	V	N	H	R	L	C	I	L	L	L	L	L	148
I3	S	I	N	S	P	K	L	C	T	C	L	V	L	L	145
I7	V	I	V	S	S	R	L	C	V	Q	M	A	A	G	152
I8	N	I	N	S	H	K	L	C	T	C	L	L	L	V	145
I9	S	I	N	S	P	K	L	C	V	S	L	V	V	L	147
I14	T	I	N	S	T	K	F	C	A	S	L	V	L	L	147
I15	S	I	N	S	P	K	L	C	V	S	L	V	V	L	147

	<u>IV</u>														
F3	S	W	I	V	S	V	L	H	A	L	F	Q	S	L	161
F5	S	W	V	V	A	N	M	N	C	L	L	H	I	L	161
F6	S	W	L	C	G	F	S	A	I	T	V	P	A	T	164
F12	S	W	V	I	S	I	F	H	A	F	I	Q	S	L	162
I3	L	W	M	L	T	T	S	H	A	M	M	H	T	L	159
I7	S	W	A	G	G	F	G	I	S	M	V	K	V	F	166
I8	F	W	I	M	T	S	S	H	A	M	M	H	T	L	159
I9	S	W	V	L	T	T	F	H	A	M	L	H	T	L	161
I14	L	W	M	L	T	M	T	H	A	L	L	H	T	L	161
I15	S	W	V	L	T	T	F	H	A	M	L	H	T	L	161

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Figur 4G

F3	M M L A L P F C T H L E I P	175
F5	L M A R K S F C A D N M I P	175
F6	L I A R L S F C G S R V I N	178
F12	I V L Q L T F C G D V K I P	176
I3	L A A R L S F C E N N V V L	173
I7	L I S R L S Y C G P N T I N	180
I8	L A A R L S F C E N N V L L	173
I9	L M A R L S F C E D S V I P	175
I14	L I A R L S F C E K N V I L	175
I15	L M A R L S F C A D N M I P	175

F3	H Y F C E P N Q V I Q L T C	189
F5	H F F C D G T P L L K L S C	189
F6	H F F C D I S P W I V L S C	192
F12	H F F C E L N Q L S Q L T C	190
I3	N F F C D L F V L L K L A C	187
I7	H F F C D V S P L L N L S C	194
I8	N F F C D L F V L L K L A C	187
I9	H Y F C D M S T L L K V A C	189
I14	H F F C D I S A L L K L S C	189
I15	H F F C D I S P L L K L S C	189

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Figur 4H

	<u>V</u>	
F3	S D A F L N D L V I Y F T L	203
F5	S D T H L N E L M I L T E G	203
F6	T D T Q V V E L V S F G I A	206
F12	S D N F P S H L I M N L V P	204
I3	S D T Y I N E L M I F I M S	201
I7	T D M S T A E L T D F V L A	208
I8	S D T Y V N E L M I H I M G	201
I9	S D T H D N E L A I F I L G	203
I14	S D I Y V N E L M I Y I L G	203
I15	S D T H V N E L V I F V M G	203

	<u>V</u>	
F3	V L L A T V P L A G I F Y S	217
F5	A V V M V T P F V C I L I S	217
F6	F C V I L G S C G I T L V S	220
F12	V M L A A I S F S G I L Y S	218
I3	T L L I I I P F F L I V M S	215
I7	I F I L L G P L S V T G A S	222
I8	V I I I V I P F V L I V I S	215
I9	G P I V V L P F L L I I V S	203
I14	G L I I I I P F L L I V M S	203
I15	G L V I V I P F V L I I V S	203

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Figur 4I

	<u>V</u>	
F3	Y F K I V S S I C A I S S V	231
F5	Y I H I T C A V L R V S S P	231
F6	Y A Y I I T T I I K I P S A	234
F12	Y F K I V S S I H S I S T V	232
I3	Y A R I I S S I L K V P S T	229
I7	Y M A I T G A V M R I P S A	236
I8	Y A K I I S S I L K V P S T	229
I9	Y A R I V S S I F K V P S S	231
I14	Y V R I F F S I L K F P S I	231
I15	Y A R V V A S I L K V P S V	231

	<u>VI</u>	
F3	H G K Y K A F S T C A S H L	245
F5	R G G W K S F S T C G S H L	245
F6	R G R H R A F S T C S S H L	248
F12	Q G K Y K A F S T C A S H L	246
I3	Q G I C K V F S T C G S H L	243
I7	A G R H K A F S T C A S H L	250
I8	Q S I H K V F S T C G S H L	243
I9	Q S I H K A F S T C G S H L	245
I14	Q D I Y K V F S T C G S H L	245
I15	R G I H K I F S T C G S H L	245

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Figur 4J

	<u>VI</u>	
F3	S V V S L F Y C T G L G V Y	259
F5	A V V C L F Y G T V I A V Y	259
F6	T V V L I W Y G S T I F L H	262
F12	S I V S L F Y S T G L G V Y	260
I3	S V V S L F Y G T I I G L Y	257
I7	T V V I I F Y A A S I F I Y	264
I8	S V V S L F Y G T I I G L Y	257
I9	S V V S L F Y G T V I G L Y	259
I14	S V V T L F Y G T I F G I Y	259
I15	S V V S L F Y G T I I G L Y	259

	<u>VI</u>	<u>VII</u>	
F3	L S S A A N N S S Q A S A T		273
F5	F N P S S S H L A G R D M A		273
F6	V R T S V E S S L D L T K A		276
F12	V S S A V V Q S S H S A A S		274
I3	L C P A G N N S T V K E M V		271
I7	A R P K A L S A F D T N K L		278
I8	L C P S G D N F S L K G S A		271
I9	L C P S A N N S T V K E T V		273
I14	L C P S G N N S T V K E I A		273
I15	L C P S A N N S T V K E T V		273

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Figur 4K

	<u>VII</u>														
F3	A	S	V	M	Y	T	V	V	T	P	M	V	N	P	287
F5	A	A	V	M	Y	A	V	V	T	P	M	L	N	P	287
F6	I	T	V	L	N	T	I	V	T	P	V	L	N	P	290
F12	A	S	V	M	Y	T	V	V	T	P	M	L	N	P	288
I3	M	A	M	M	Y	T	V	V	T	P	M	L	N	P	285
I7	V	S	V	L	Y	A	V	I	V	P	L	F	N	P	292
I8	M	A	M	M	Y	T	V	V	T	P	M	L	N	P	285
I9	M	S	L	M	Y	T	M	V	T	P	M	L	N	P	287
I14	M	A	M	M	Y	T	V	V	T	P	M	L	N	P	287
I15	M	A	M	M	Y	T	V	V	T	P	M	L	N	P	287

	<u>VII</u>														
F3	F	I	Y	S	L	R	N	K	D	V	K	S	V	L	301
F5	F	I	Y	S	L	R	N	S	D	M	K	A	A	L	301
F6	F	I	Y	T	L	R	N	K	D	V	K	E	A	L	304
F12	F	I	Y	S	L	R	N	K	D	V	K	R	A	L	302
I3	F	I	Y	S	L	R	N	R	D	M	K	R	A	L	299
I7	I	I	Y	C	L	R	N	Q	D	V	K	R	A	L	306
I8	F	I	Y	S	L	R	N	R	D	M	K	Q	A	L	299
I9	F	I	Y	S	L	R	N	R	D	I	K	D	A	L	301
I14	F	I	Y	S	L	R	N	R	D	M	K	R	A	L	301
I15	F	I	Y	S	L	R	N	R	D	M	K	E	A	L	301

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Figur 4L

F3	K K T L C E E V I R S P P S	315
F5	R K V L A M R F P S K Q -	313
F6	R R T V K G K -	311
F12	E R L L E G N C K V H H W T	316
I3	I R V I C S M K I T L -	310
I7	R R T L H L A Q D Q E A N T	320
I8	I R V T C S K K I S L P W -	312
I9	E K I M C K K Q I P S F L -	314
I14	I R V I C T K K I S L -	312
I15	I R V L C K K K I T F C L -	314

F3	L L H F F L V L C H L P C F	329
F5		
F6		
F12	G -	317
I3		
I7	N K G S K I G -	327
I8		
I9		
I14		
I15		

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Figure 4M

F3 I F C Y -
F5
F6
F12
I3
I7
I8
I9
I14
I15

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Figure 6A(2)

	V
F2	L V L P F A L I I M S Y V R
F3	A T V P L A G I F Y S Y F K
F5	M V T P F V C I L I S Y I H
F6	I H G S C G I T L V S Y A Y
F7	L V I P F V L I I V S Y V R
F8	A A I S L S G I L Y S Y F K
F12	A A I S F S G I L Y S Y F K
F13	A A I S F S G I L Y S Y F K
F23	A V V P L L G I L Y S Y S K
F24	L I S S L L V V L V S Y L F
I3	I I I P F F L I V M S Y A R
I7	L L G P L S V T G A S Y M A
I8	I V I P F V L I V I S Y A K
I9	V V L P F L L I I V S Y A R
I11	M V T P F V C I L I S Y I H
I12	G A I S L S G I L Y S Y F K
I14	I I I P F L L I V M S Y V R
I15	I V I P F V L I I V S Y A R

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Figure 6A(3)

F2	I	V	S	S	I	L	K	V	P	S	S	Q	G	I
F3	I	V	S	S	I	C	A	I	S	S	V	H	G	K
F5	I	T	C	A	V	L	R	V	S	S	P	R	G	G
F6	I	I	T	T	I	I	K	I	P	S	A	R	G	R
F7	I	V	S	S	I	L	K	V	P	S	A	R	G	I
F8	I	V	S	S	I	R	S	M	S	S	V	Q	G	K
F12	I	V	S	S	I	H	S	I	S	T	V	Q	G	K
F13	I	V	S	S	I	R	S	V	S	S	V	K	G	K
F23	I	V	S	S	I	R	A	I	S	T	V	Q	G	K
F24	I	L	I	A	I	L	R	M	N	S	A	E	G	R
I3	I	I	S	S	I	L	K	V	P	S	T	Q	G	I
I7	I	T	G	A	V	M	R	I	P	S	A	A	G	R
I8	I	I	S	S	I	L	K	V	P	S	T	Q	S	I
I9	I	V	S	S	I	F	K	V	P	S	S	Q	S	I
I11	I	T	W	A	V	L	R	V	S	S	P	R	G	G
I12	I	V	S	S	V	R	S	I	S	S	V	Q	G	K
I14	I	F	F	S	I	L	K	F	P	S	I	Z	D	I
I15	V	V	A	S	I	L	K	V	P	S	V	R	G	I

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Figure 6A(4)

F2	Y	K
F3	Y	K
F5	W	K
F6	H	R
F7	R	K
F8	Y	K
F12	Y	K
F13	Y	K
F23	Y	K
F24	R	K
I3	C	K
I7	H	K
I8	H	K
I9	H	K
I11	W	K
I12	H	K
I14	Y	K
I15	H	K

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Figure 6B

					<u>V</u>										
F12	F	P	S	H	L	I	N	N	L	V	P	V	M	L	
F13	F	P	S	H	L	I	N	N	L	V	P	V	M	L	
F8	F	P	S	H	L	T	N	H	L	V	P	V	I	L	
I12	F	P	S	H	L	I	N	N	L	V	P	V	M	L	
F23	F	L	N	D	V	I	N	Y	F	A	L	V	L	L	
F3	F	L	N	D	L	V	I	Y	F	T	L	V	L	L	

						<u>V</u>									
F12	A	A	I	S	F	S	G	I	L	Y	S	Y	F	K	
F13	A	A	I	S	F	S	G	I	L	Y	S	Y	F	K	
F8	A	A	I	S	L	S	G	I	L	Y	S	Y	F	K	
I12	G	A	I	S	L	S	G	I	L	Y	S	Y	F	K	
F23	A	V	V	P	L	L	G	I	L	Y	S	Y	S	K	
F3	A	T	V	P	L	A	G	I	F	Y	S	Y	F	K	

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Figure 6B (Continued)

F12	I	V	S	S	I	H	S	I	S	T	V	Q	G	K
F13	I	V	S	S	I	R	S	V	S	S	V	K	G	K
F8	I	V	S	S	I	R	S	M	S	S	V	Q	G	K
I12	I	V	S	S	V	R	S	I	S	S	V	Q	G	K
F23	I	V	S	S	I	R	A	I	S	T	V	Q	G	K
F3	I	V	S	S	I	C	A	I	S	S	S	H	G	K

F12	Y	K
F13	Y	K
F8	Y	K
I12	H	K
F23	Y	K
F3	Y	K

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Figure 6C

					<u>V</u>													
F7	H	V	N	E	L	V	I	F	V	M	G	G	I	I				
I15	H	V	N	E	L	V	I	F	V	M	G	G	L	V				
I3	Y	I	N	E	L	M	I	F	I	N	S	T	L	L				
I8	Y	V	N	E	L	M	I	H	I	N	G	V	I	I				
I9	H	D	N	E	L	A	I	F	I	L	G	G	P	I				
I14	Y	V	N	E	L	M	I	Y	I	L	G	G	L	I				

						<u>V</u>											
F7	L	V	I	P	F	V	L	I	I	V	S	Y	V	R			
I15	I	V	I	P	F	V	L	I	I	V	S	Y	A	R			
I3	I	I	I	P	F	F	L	I	V	M	S	Y	A	R			
I8	I	V	I	P	F	V	L	I	V	I	S	Y	A	K			
I9	V	V	L	P	F	L	L	I	I	V	S	Y	A	R			
I14	I	I	I	P	F	L	L	I	V	M	S	Y	V	R			

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Figure 6C (Continued)

F7	I	V	S	S	I	L	K	V	P	S	A	R	G	I
I15	V	V	A	S	I	L	K	V	P	S	V	R	G	I
I3	I	I	S	S	I	L	K	V	P	S	T	Q	G	I
I8	I	I	S	S	I	L	K	V	P	S	T	Q	S	I
I9	I	V	S	S	I	F	K	V	P	S	S	Q	S	I
I14	I	F	F	S	I	L	K	F	P	S	I	Q	D	I

F7	R	K
I15	H	K
I3	C	K
I8	H	K
I9	H	K
I14	Y	K

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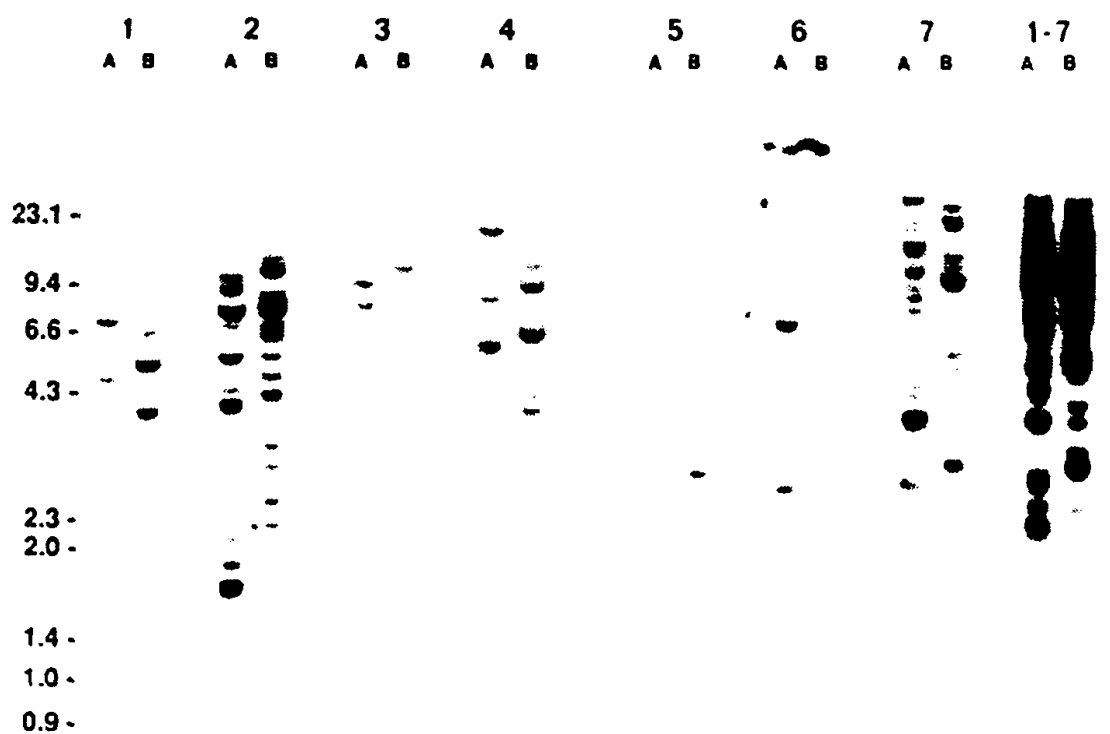
Figure 6D

[illegible][illegible]

F5 I T C A V L R V S S P R G G
I11 I T W A V L R V S S P R G G

F5 W K
I11 W K

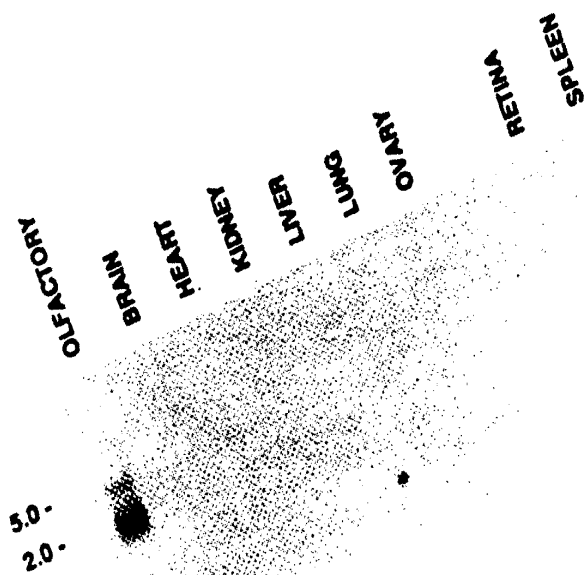
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Figure 7

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Figure 8

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Figure 9A Translated sequence of F3T.D1S

10	20	30	40	50	60
* ATG GAC TCA AGC AAC AGG ACA AGA GTT TCA GAA TTT CTT CTT GGA TTT GTA GAA AAC	* M D S S N R T R V S E F L L C F V E N	* 70	* 80	* 90	* 100
* AAA GAC CTA CAA CCC CTT ATT TAT GGT CTT TTT CTC TCT ATG TAC CTG GTT ACT GTC ATT	* K D L Q P L I Y G L F L S M Y L V T V I	* 130	* 140	* 150	* 160
* CGA AAC ATA TCC ATT ATT CTG GCT ATC ATT TCA GAT CCC TGT CTG CAC ACC CCC ATG TAT	* G N I S I I V A I I S D P C L H T P M Y	* 190	* 200	* 210	* 220
* TTC TTC CTC TCT AAC CTG TCC TTT GTG GAC ATC TGT TTC ATT TCA ACC ACT GTT CCA AAC	* F F L S N L S F V D I C F I S T T V P K	* 250	* 260	* 270	* 280
* ATG TTA GTG AAC ATC CAG ACC CAA AAC AAT GTC ATC ACC TAT GCA GGA TGC ATT ACC CAG	* M L V N I Q T Q N N V I T Y A C C I T Q				

Figure 9B

ATA TAC TTT TTC TTG CTC TTT GTA GAA TTG GAC AAC TTC TTG CTG ACT ATC ATG GCC TAT	310	320	330	340	350	360
I Y F F L L L F V E L D N F L L L T I M A Y	*	*	*	*	*	*
GAC CGT TAC GTA GCC ATC TGT CAC CCC ATG CAC TAC ACA GTT ATC ATG AAC TAC AAG CTC	370	380	390	400	410	420
D R Y V A I C H P M H Y T V I M N Y K L	*	*	*	*	*	*
TGT GGA TTT CTG GTT CTG GTA TCT TGG ATT GTA AGT GTT CTG CAT GCC TTT TTT CAA AGC	430	440	450	460	470	480
C G F L L V L V S S W I V S V L H A L F Q S	*	*	*	*	*	*
TTG ATG ATG TTG GCG CTG CCC TTC TGC ACA CAT CTG GAA ATC CCA CAC TAC TTC TGT GAA	490	500	510	520	530	540
L M M L L A L L P F C T H L E I P H Y F C E	*	*	*	*	*	*
CCT AAT CAG CTG ATT CAA CTC ACC TGT TCT GAT GCA TTT CTT AAT GAT CTT CTG ATA TAT	550	560	570	580	590	600
P N Q V I Q L L T C S D A F L N D L V I Y	*	*	*	*	*	*
	610	620	630	640	650	660

Figure 9C

TTT	ACA	CTT	GTG	CTG	CTG	GCT	ACT	GTT	CCT	CCT	GCT	GCT	ATC	TTC	TAT	TCT	TAC	TTC	AAG	*
F	T	L	V	L	L	A	T	V	P	P	L	A	G	I	F	Y	S	Y	F	K
670						680			690				700			710			720	
*						*			*				*			*			*	
ATA	GTG	TCC	TCC	ATA	TGT	GCT	ATA	TCG	TCA	GTT	CAT	GGG	AAG	TAC	AAA	GCA	TTC	TCC	ACC	
I	V	S	S	I	C	A	I	S	S	V	H	G	K	Y	K	A	F	S	T	
730						740			750				760			770			780	
*						*			*				*			*			*	
TGT	GCA	TCT	CAC	CTT	TCA	GTC	GTG	TCT	TTA	TTT	TAC	TGC	ACA	GGA	CIA	GGA	GTG	TAC	CTC	
C	A	S	H	L	S	V	V	S	L	F	Y	C	T	G	L	G	V	Y	L	
790						800			810				820			830			840	
*						*			*				*			*			*	
AGT	TCT	GCT	GCA	AAC	AAC	AGC	TCA	CAG	GCA	AGT	GCC	ACA	GCC	TCA	GTC	ATG	TAC	ACT	GTA	
S	A	A	A	N	N	S	S	Q	A	S	A	T	A	S	V	M	Y	T	V	
850						860			870				880			890			900	
*						*			*				*			*			*	
GTT	ACC	CCT	ATG	GTG	AAC	CCT	TTT	ATC	TAT	AGT	CTT	AGG	AAT	AAA	CAT	GTT	AAG	AGT	GTT	
PRONUC/TRA OPTION																				
V	T	P	M	V	N	P	F	I	Y	S	L	R	N	K	D	V	K	S	V	

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Figure 9D

CTG AAA ACT CTT TGT GAG GAA GTT ATA AGG AGT CCA CCT TCC CTA CTT CAT TTC TTC	910	920	930	940	950	960
L K T L C E E V I R S P P S L L H F F	*	*	*	*	*	*
CTA GTG TTA TGT CAT CTC CCT TGT TTT ATT TTT TGT TAT TAA	970	980	990	1000		
L V L C H L P C F I F C Y -	*	*	*	*		

Translation begun with base no. 57

Translated to base no.1058

Sequence printed from base no. 57 to base no.1058

Sequence numbered beginning with base no. 57

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Figure 10A Translated sequence of F5T.D1S

10	20	30	40	50	60
* ATG AGC AGC ACC AAC CAG TCC AGT GTC ACC GAG TTC CTC CTC CTG GGA CTC TCC AGG CAG	* M S S T N Q S S S V T E F L L L G L S R Q	* 70	* 80	* 90	* 100
* CCC CAG CAG CAG CTC CTC TTC CTC CTC TTC CTC ATC ATG TAC CTG GCC ACT CTC CTC	* P Q Q Q Q L L F L F L L I M Y L A T V L	* 130	* 140	* 150	* 160
* GGA AAC CTG CTC ATC ATC CTG GCT ATT GGC ACA GAC TCC CGC CTG CAC ACC CCC ATG TAC	* G N L L I I L L A I G T D S R L H T P M Y	* 190	* 200	* 210	* 220
* TTC TTC CTC AGT AAC CTG TCC TTT GTG GAT GTC TGC TTC TCC TCT ACC ACT GTC CCT AAA	* F F L S N L S F V D V C F S S S T T V P K	* 250	* 260	* 270	* 280
* CTT CTG GCC AAC CAT ATA CTT GGG AGT CAG GCC ATT TCC TTC TCT GGG TGT CTC ACC CAG	* V L A N H I L L G S Q A I S F S G C L T Q				

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Figure 10B

CTG TAT TTT CTC GCT GTC TTT GGT AAC ATG GAC AAT TTC CTG CTG GCT CTG ATG TCC TAT	310	320	330	340	350	360
L Y F L A V F G N M D N F L L A V M S Y	*	*	*	*	*	*
GAC CGA TTT GTG GCC ATA TGC CAC CCT TTA CAC TAC ACA AAG ATG ACC CGT CAG CTC	370	380	390	400	410	420
D R F V A I C H P L H Y T T K M T R Q L	*	*	*	*	*	*
IGT GTC CTG CTT GTT GTG GGG TCA TGG GTT GTA GCC AAC ATG AAT TGT CTG TTG CAC ATA	430	440	450	460	470	480
C V L L V V G G S W V V A N M N C L L H I	*	*	*	*	*	*
CTG CTC ATG GCT CGA CTC TCC TCC TTC TGT GCA GAC AAC ATG ATC CCC CAC TTC TTC TGT GAT	490	500	510	520	530	540
L L M A R L S S F C A D N M I P H F C D	*	*	*	*	*	*
GGA ACT CCC CTC CTG AAA CTC TCC TGC TCA GAC ACA CAT CTC AAT GAG CTG ATG ATT CTT	550	560	570	580	590	600
G T P L L K L S C S D T H L L N E L M I L	*	*	*	*	*	*
	610	620	630	640	650	660

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Figure 10C

ACA GAG GGA GCT GTG GTC ATG GTC ACC CCA TTT GTC TGC ATC CTC ATC TCC TAC ATC CAC	*	*	*	*	*	*	*
T E G A V V M V V V T P F V C I L I S Y I H							
670	680	690	700	710	720		
ATC ACC TGT GCT CTC AGA GTC TCA TCC CCC AGG GGA GGA TGG AAA TCC TTC TCC ACC	*	*	*	*	*		
I T C A V L R V S S S P R G G W K S F S T							
730	740	750	760	770	780		
TGT GGC TCC CAC CTG GCT GTG GTC TGC CTC TTC TAT GGC ACC GTC ATC GCT GTG TAT TTC	*	*	*	*	*		
C G S H L A V V C L F Y G T V I A V Y F							
790	800	810	820	830	840		
AAC CCA TCA TCC TCT CAC TTA GCT GGG AGG GAC ATG GCA GCT GCA GTG ATG TAT GCA GTG	*	*	*	*	*		
PRONUC/TRA OPTION							
N P S S S H L A G R D M A A A V M Y A V							

Figure 10D

850	*	860	*	870	*	880	*	890	*	900	*
GTG ACC CCA ATG CTG AAC CCT TTC ATC TAT AGC CTG AGG AAC AGC GAC ATG AAA GCA GCT											
V T P M L N P F I Y S L R N S D M K A A											
910	*	920	*	930	*	940	*				
TTA AGG AAA GTG CTC GCC ATG AGA TTT CCA TCT AAG CAG TAA											
L R K V L A M R F P S K Q -											

Translation begun with base no. 62

Translated to base no.1003

; Sequence printed from base no. 62 to base no.1003

Sequence numbered beginning with base no. 62

Figure 11A Translated sequence of F6T.D1S

10	20	30	40	50	60
* ATG GCT TGG AGT ACT GGC CAG AAC CTG TCC ACA CCA GGA CCA TTC ATC TTG CTG GGC TTC M A W S T G Q N L S T P G P F I L L G F	* 80	* 90	* 100	* 110	* 120
* CCA GGG CCA AGG AGC ATG CGC ATT GGG CTC TTC CTG CTT TTC CTG GTC ATG TAT CTG CTT P G P R S M R I G L F L L F L V M Y L L	* 140	* 150	* 160	* 170	* 180
* ACG GTA GTT GGA AAC CTA GCC ATC ATC TCC CTC GTA GGT GCC CAC AGA TGC CTA CAG ACA T V V G G N L A I I S L V G A H R C L Q T	* 200	* 210	* 220	* 230	* 240
* CCC ATG TAC TTC TTC TGC AAC CTC TCC TTC CTG GAG ATC TGG TTC ACC ACA GCC TGC P M Y F F L C N L S F L E I W F T A C	* 260	* 270	* 280	* 290	* 300
* GTA CCC AAG ACC CTG GCC ACA TTT GCG CCT CGG GGT GGA GTC ATT TCC TTG GCT GGC TGT V P K T L A T F A P R G G V I S L A G C					

Figure 11B

310	320	330	340	350	360
* GCC ACA CAG ATG TAC TTT GTC TTT TCT TTG GGC TGT ACC GAG TAC TTC CTG CTG GCT CTG	* A T Q M Y F V F S L G C T E Y F L L A V	* 330	* 340	* 350	* 360
370	380	390	400	410	420
* ATG GCT TAT GAC CGC TAG CTG GGC ATC TGC CTG CCA CTG GGC TAT GGT GGC ATC ATG ACT	* M A Y D R Y L A I C L P L R Y C G I M T	* 390	* 400	* 410	* 420
430	440	450	460	470	480
* CCT GGG CTG GCG ATG CGG TTG GGC CTG GGA TCC TGG CTG TGT GGC TTT TCT GCA ATC ACA	* P G L A A M R L A L G S W L C G F S A I T	* 450	* 460	* 470	* 480
490	500	510	520	530	540
* GTT CCT GCT ACC CTC ATT GCC CGC CTC TCT TTC TGT TGT GGC TCA CGT GTC ATC AAC CAC TTC	* V P A T L I A R L S F C G S R V I N H F	* 510	* 520	* 530	* 540
550	560	570	580	590	600
* TTC TGT GAC ATT TCG CCC TGG ATA CTG CTT TCC TGC ACC GAC ACC GAG CTG GTG GAA CTG	* F C D I S P W I V L S C T D T Q V V E L	* 570	* 580	* 590	* 600
610	620	630	640	650	660

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Figure 11c

* GCG	* TTC	* GTT	* CTG	* GGC	* TCG	* TGT	* GGT	* ATC	* ACA	* CTA	* GTC	* TCC
V S F	G I A	F C V	I L G	S C G	I T L	V S						
670	680	690	700	710	720							
* TAT	* GCT	* TAC	* ATC	* ATC	* ACC	* ATC	* AAG	* ATT	* CCC	* TCT	* GCC	* CGG
Y A Y	I I I	T T T	I I I	K I P	A S A	R G R	H R A					
730	740	750	760	770	780							
* TTC	* TCA	* TCC	* CAT	* CTC	* CTG	* CTG	* TAT	* TGG	* TCC	* ACC	* ATC	* TTC
F S T	C C S	H S S	V L V	I L I	W Y G	T I T	S I F					
790	800	810	820	830	840							
* TTG	* CAT	* GTG	* ACC	* TCG	* GTA	* GAG	* AGC	* TCC	* TTC	* GAC	* CTC	* ACC
PRONUC/TRA	OPTION											
L H V	R T S	V E S	S S L	T L D	K A I	T V L						

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Figur 11D

850	*		860	*		870	*		880	*		890	*		900	*
AAC ACC ATT GTC ACA CCT GTG CTG AAC CCT TTC ATA TAT ACT CTG AGG AAC AAG GAT GTC																
N T I V T P V L N P F I Y T L R N K D V																

910	*		920	*		930	*
AAG GAA GCT CTG CGC AGG ACC GTG AAG GGG AAG TGA							
K E A L R R T V K G K -							

Translation begun with base no. 75

Translated to base no.1010

Sequence printed from base no. 75 to base no.1010

Sequence numbered beginning with base no. 75

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Figure 12A Translated sequence of F12T.D1S

10	20	30	40	50	60
* ATG GAA TCA GGG AAC AGC ACA AGA AGA TTT TCA AGT TTT TTT CTT CTT GGA TTT ACA GAA M E S G N S T R R F S S F F L L G F T E	* 70	* 80	* 90	* 100	* 110
* AAC CCA CAA CTT CAC TTC CTC ATT TTT GCA CTA TTC CTG TCC ATG TAC CTG GTA ACA GTG N P Q L L H F L I F A L F L S M Y L V T V	* 130	* 140	* 150	* 160	* 170
* CTT GGG AAC CTG CTT ATC ATT ATG GCC ATC ATC ACA CAG TCT CAT TTG CAT ACA CCC ATG L G N L L L I I M A I I T Q S H L H T P M	* 190	* 200	* 210	* 220	* 230
* TAC TTT TTC CTT GCT AAC CTA TCC TTT GTG GAC ATC TGT TTC ACC TCG ACC ACC ATC CCA Y F F L A N L S F V D I C F T T S T I P	* 250	* 260	* 270	* 280	* 290
					* 300

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Figure 12B

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AAG ATG TTG GTA AAT ATA TAC ACC CAG AGC AAG AGC ATC ACC TAT GAA GAC TGT ATT AGC
K M L V N I Y T Q S K S I T Y E D C I S

310 * 320 * 330 * 340 * 350 * 360 *
CAG ATG TGT GTC TTC TTG GTT TTC GCA GAA TTG GGC AAC TTT CTC CTG GCT GTG ATG GCC
Q M C V F L V F A E L G N F L L A V M A

370 * 380 * 390 * 400 * 410 * 420 *
TAT GAC CGA TAT GTG GCT A-C TGT CAC CCA CTG TGT TAC ACA GTC ATT GTG AAC CAC CCG
Y D R Y V A X C C H P L C Y T V I V N H R

430 * 440 * 450 * 460 * 470 * 480 *
CTC TGT ATC CTG CTG CTT CTG CTG TCC TGG GTT ATC AGC ATT TTC CAT GCC TTC ATA CAG
L C I L L L L L S W V I S I F H A F I Q

490 * 500 * 510 * 520 * 530 * 540 *
AGC TTA ATT GTG CTA CAG TTG ACC TTC TGT TGT GGA GAT GTG AAA ATC CCT CAC TTC TTC TGT
S L I V L Q L L T F C C G D V K I P H F F C

550 * 560 * 570 * 580 * 590 * 600 *
GAA CTT AAT CAG CTG TCC CAA CTC ACC TGT TCA GAC AAC TTT CCA AGT CAC CTC ATA ATG
E L N Q L L S Q Q L T C S D N F P S H L I M

```

Figure 12C

610	*	620	*	630	*	640	*	650	*	660	*
AAT CTT GTA CCT GTT ATG TTG GCA GCC ATT TCC TTC AGT GGC ATC CTT TAC TCT TAT TTC											
N L V P V M L A A I S F S G I L Y S Y F											
670	*	680	*	690	*	700	*	710	*	720	*
AAG ATA GTA TCC TCC ATA CAT TCT ATC TCC ACA GTT CAG GCG AAG TAC AAG GCA TTT TCT											
K I V S S I H S I S T V Q G K Y K A F S											
730	*	740	*	750	*	760	*	770	*	780	*
ACT TGT GCC TCT CAC CTT TCC ATT GTC TCC TTA TTT TAT AGT ACA GGC CTC GGA GTG TAC											
T C A S H L S I V S L L F Y S T G L G V Y											
790	*	800	*	810	*	820	*	830	*	840	*
GTC AGT TCT GCT GTG GTC CAA AGC TCA CAT TCT GCT GCA AGT GCT TCG GTC ATG TAT ACT											
PRONUC/TRA OPTION											
V S S A V V Q S S H S A A S A S V M Y T											

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Figure 12D

850	860	870	880	890	900
* GTG GTC ACC CCC ATG CTG AAC CCC TTC ATT TAT AGT CTA AGG AAT AAA GAT CTG AAG AGA	* V V T P M L N P F I Y S L R N K D V K R	* 910	* 920	* 930	* 940
* GCT CTG GAA AGA CTG TTA GAA GGA AAC TGT AAA CTG CAT TGG ACT GGA TGA	* A L E R L L E G N C K V H H T G -				

Translation begun with base no. 173

Translated to base no. 1126

Sequence printed from base no. 173 to base no. 1126

Sequence numbered beginning with base no. 173

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Figure 13A Translated sequence of I3T.D1S

10	20	30	40	50	60
* ATG AAC AAT CAA ACT TTC ATC ACC CAA TTC CTT CTC CTG GGA CTG CCC ATC CCT GAA GAA M N Q T F I T Q F L L L G L P I P E E	* 70	* 80	* 90	* 100	* 110
* CAT CAG CAC CTG TTC TAT GCC TTG TTC CTG GTC ATG TAC CTC ACC ACC ATC TTG GGA AAC H Q H L F Y A L F L V M Y L L T T I L G N	* 130	* 140	* 150	* 160	* 170
* TTG CTA ATC ATT GTA CTT GTT CAA CTG GAC TCC CAG CTC CAC ACA CCT ATG TAT TTG TTT L L I I V L V Q L D S Q L H T P M Y L F	* 190	* 200	* 210	* 220	* 230
* CTC AGC AAT TTG TCT TTC TCT GAT CTA TGT TTT TCC TCT GTC ACA ATG CCC AAG CTG CTG L S N L S F S D L C F S S V T M P K L L	* 250	* 260	* 270	* 280	* 290
* CAG AAC ATG AGG AGC CAG GAC ACA TCC ATT CCC TAT GGA GGC TGC CTG GCA CAA ACA TAC Q N M R S S Q D T S I P Y G G C L A Q T Y					

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Figure 13B

310	320	330	340	350	360
TTC TTT ATG GTT TTT GGA GAT ATG GAG AGT TTC CTT CTT GTG GCC ATG GCC TAT GAC CGC	*	*	*	*	*
F F M V F F G D M E S F L L V A M A Y D R					
370	380	390	400	410	420
TAT GTG GCC ATO TGC TTC CCT CTG CAT TAC ACC AGC ATC ATG AGC CCC AAG CTC TGT ACT	*	*	*	*	*
Y V A I C F P L H Y T S I M S P K L C T					
430	440	450	460	470	480
TGT CTA GTG CTG TTA TTG TGG ATG CTG ACG ACA TCC CAT GCC ATG ATG CAC ACA CTG CTT	*	*	*	*	*
C L V L L L L W M L T T S H A M M H T L L					
490	500	510	520	530	540
GCA GCA AGA TTG TCT TTT TGT TGT GAG AAC AAT GTG GTC CTC AAC TTC TTC TGT GAC CTA TTT	*	*	*	*	*
A A R L L S F C C E N N V V L N F F C D L F					
550	560	570	580	590	600
GTT CTC CTA AAG CTG GCC TGC TCA GAC ACT TAT ATT AAT GAG TTG ATG ATA TTT ATC ATG	*	*	*	*	*
V L L K L L A C S D T Y I N E L M I F I M					
610	620	630	640	650	660

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Figur 13C

AGT AÇA CTC CTC ATT ATT ATT CCA TTC TTC CTC ATT GTT ATG TCC TAT GCA AGG ATC ATA	*	*	*	*	*	*	*
S T L L I I I I P F F F L I V M S Y A R I I							
670	680	690	700	710	720		
TCC TCT ATT CTT AAG GTT CCA TCT ACC CAA GGC ATC TGC AAG GTC TTC TCT ACC TGT GGT	*	*	*	*	*		
S S I L K V P P S S T Q G I C K V F S T C G							
730	740	750	760	770	780		
TCC CAT CTG TCT GTA GTA TCA CTG TTC TAT GGG ACA ATT ATT GGT CTC TAC TTA TGT CCA	*	*	*	*	*		
S H L S V V S S L F Y G T I I G L Y L C P							

Figure 14A Translated sequence of I7T.D1S

10	20	30	40	50	60
* ATG GAG CGA AGG AAC CAC AGT GGG AGA GTG AGT GAA TTT GTG TTG CTG GGT TTC CCA GCT					*
M E R R N H S G C R V S E F V L L G F P A					
70	80	90	100	110	120
* CCT GCC CGA CTG CGA GTA CTA CTA TTT TTC CTT TCT TCT G-C TAT GTG TTG GTG TTG				*	*
P A P L R V L L L F F L S L L X Y V L V L					
130	140	150	160	170	180
* ACT GAA AAC ATG CTC ATC ATT ATA GCA ATT AGG AAC CAC CCA ACC CTC CAC AAA CCC ATG				*	*
T E N M L I I I I A I R N H P T L H K P M					
190	200	210	220	230	240
* TAT TTT TTC TTG GCT AAT ATG TCA TTT CTC GAG ATT TGG TAT GTG ACT GTT ACG ATT CCT				*	*
Y F F L A N M S F L E I W Y V T V T I P					
250	260	270	280	290	300
* AAG ATG CTC GCT GGC TTC ATT GGT TCC AAG GAG AAC CAT GCA CAG CTG ATC TCC TTT GAG				*	*
K M L A G G F I G S K E N H G Q L I S F E					

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Figure 14B

310	320	330	340	350	360
* GCA TGC ATG ACA CAA CTC TAC TTT TTC CTG GGC TTG GGT TGC ACA GAG TGT GTC CTT CTT	* A C M T Q L Y F F L G L G C T E C V L L	*	*	*	*
370	380	390	400	410	420
* GCT GTG ATG GCC TAT GAC CGC TAT GTG GCT ATC TGT CAT CCA CTC CAC TAC CCC GTC ATT	* A V M A Y D R Y V A I C H P L H Y P V I	*	*	*	*
430	440	450	460	470	480
* GTC AGT AGC CGG CTA TGT GTG CAG ATG GCA GCT GGA TCC TGG GCT GGA GGT TTT GGT ATC	* V S S R L C V Q M A A G S W A G G F G I	*	*	*	*
490	500	510	520	530	540
* TCC ATG GTT AAA GTT TTC CTT ATT TCT CGC CTG TCT TAC TGT TGT GGC CCC AAC ACC ATC AAC	* S M V K V F L I S R L S Y C G P N T I N	*	*	*	*
550	560	570	580	590	600
* CAC TTT TTC TGT GAT GTG TCT CCA TTG CTC AAC CTG TCA TGC ACT GAC ATG TCC ACA GCA	* H F F C D V S P L L N L S C T D M S T A	*	*	*	*

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Figure 14C

610	620	630	640	650	660														
* GAG CTT ACA GAC TTT CTC CTG GGC ATT TTT ATT CTG GGA CCG CTC TCT GTC ACT GGC	* E L T D F V L A I F I L L L G P L S V T G	*	*	*	*														
670	680	690	700	710	720														
* GCA TCC TAC ATG GCC ATC ACA GGT GCT GTG ATG CGC ATC CCC TCA GCT GCT GGC CGC CAT	* A S Y M A I T G A V M R I P S A A G R H	*	*	*	*														
730	740	750	760	770	780														
* AAA GCC TTT TCA ACC TGT GCC TCC CAG CTC ACT GTT GTG ATC ATC TTC TAT GCA GCC ACT	* K A F S T C A S H L T V V I I F Y A A S	*	*	*	*														
790	800	810	820	830	840														
* ATT TTC ATC TAT GCC AGG CCT AAG GCA CTC TCA GCT TTT GAC ACC AAC AAG CTG GTC TCT	* I F I Y A A R P K A L S A F D T N K L V S	*	*	*	*														
850	860	870	880	890	900														
* GTA CTC TAC GCT GTC ATT GTA CCG TTG TTC AAT CCC ATC ATC TAC TGC TTG CGC AAC CAA	* PRONUC/TRA OPTION	*	*	*	*														
V	L	Y	A	V	I	V	P	L	F	N	P	I	I	Y	C	L	R	N	Q

Figure 14D

910	*	920	*	930	*	940	*	950	*	960	*
CAT GTC AAA AGA GCG CTA CGT CGC ACG CTG CAC CTG GCC CAG GAC CAG CAG GCC AAT ACC											
D V K R A L R R T L H L A Q D Q E A N T											
970	*	980	*								
AAC AAA GGC AGC AAA ATT GGT TAG											
N K G S K I G -											

Translation begun with base no. 119

Translated to base no. 1102

Sequenc printed from base no. 119 to base no. 1102

Sequence numbered beginning with base no. 119

53/98

Figure 15A Translated sequence of I8T.D1S

10	20	30	40	50	60
* ATG AAC AAC AAA ACT GTC ATC ACC CAT TTC CTC CTC CTG GGA TTG CCC ATC CCC CCA GAG	* M N N K T V I T H F L L L G L P I P P E	* 70	80	90	100
* CAC CAG CAA CTG TTC TTT GGC CTG TTC CTG ATC ATG TAC CTC ACC ACC TTT CTG GGA AAC	* H Q Q L F F A L F L I M Y L T T F L G N	110	120	130	140
* CTG CTA ATT GTT GTC CTT GTT CAA CTG GAC TCT CAT CTC CAC ACA CCC ATG TAC TTG TTT	* L L I V V L V Q L D S H L H T P M Y L F	150	160	170	180
190	200	210	220	230	240
* CTC AGC AAC TTG TCC TTC TCT GAT CTC TCC TTT TCC TCT GTT ACA ATG CTG AAA TTG CTC	* L S N L S F S D L C F S S V T M L K L L	250	260	270	280
* CAA AAT ATA CAG AGC CAA GTA CCA TCT ATA TCC TAT GCA GGA TCC CTG ACA CAG ATA TTC	* Q N I Q S S Q V P S I S Y A G C L T Q I F	290	300	310	320

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Figur 15B

TTC TTT TTG TTG TTT GGC TAC CTT GCG AAT TTC CTT CTT GTA GCC ATG GCC TAT GAC CGC	310	320	330	340	350	360
F L L F F G Y L L G N F L L V A M A Y D R	*	*	*	*	*	*
TAT CTG GCC ATC TGC TTT GGC TTT CCT CTG CAT TAT ACC AAC ATC ATG AGC CAT AAG CTC TGT ACT	370	380	390	400	410	420
Y V A I C F P L H Y T N I M S H K L C T	*	*	*	*	*	*
TGT CTC CTG CTG GTA TTT TGG ATA ATG ACA TCA TCT CAT GCC ATG ATG CAC ACC CTG CTT	430	440	450	460	470	480
C L L L V F W I M T S S S H A M M H T L L	*	*	*	*	*	*
GCA GCA AGA TTG TCT TTT TGT GAG AAC AAT GTA CTC CTC AAC TTT TTC TGT GAC CTG TTT	490	500	510	520	530	540
A A R L S F C E N N V L L L N F F C D L F	*	*	*	*	*	*
GTT CTC CTA AAG TTG GCC TGC TCA GAC ACT TAT GTT AAT GAG TTG ATG ATA CAT ATC ATG	550	560	570	580	590	600
V L L K L A C S D T Y V N E L M I H I M	*	*	*	*	*	*
	610	620	630	640	650	660

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Figure 15C

GGC GTG ATC ATC ATT GTT ATT CCA TTC GTG CTC ATT GTT ATA TCC TAT GCC AAG ATC ATC	*	*	*	*	*	*	*
G V I I I V I V I P F V V L I I V I S Y A K I I							
670	680	690	700	710	720		
TCC TCC ATT CTT AAG GTT CCA TCT ACT CAA AGC ATT CAC AAG GTC TTC TCC ACT TGT GGT	*	*	*	*	*		
S S I L K V P S T Q S I H K V F S T C G							
730	740	750	760	770	780		
TCT CAT CTC TCT GTG GTG TCT TCT CTG TTC TAC GGG ACA ATT ATT GGT CTC TAT TTA TGT CCA	*	*	*	*	*		
S H L S V V S L F Y G T I I I G L Y L C P							
790	800	810	820	830	840		
TCA GGT GAT AAT TTT AGT CTA AAG GGG TCT GCC ATG GCT ATG ATG TAC ACA GTG GTA ACT	*	*	*	*	*		
PRONUC/TRA OPTION							
S G D N F S L K G S A M A M M Y T V V T							
850	860	870	880	890	900		
CCA ATG CTG AAC CCG TTC ATC TAC AGC CTA AGA AAC AGA GAC ATG AAG CAG GCC CTA ATA	*	*	*	*	*		
P M L N P F I Y S L R N R D M K Q A L I							

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Figure 15D

	910		920		930		9
	*		*		*		
AGA	GTT	ACC	TGT	AGC	AAG	AAA	ATC
R	V	T	C	S	K	K	I
							S
							L
							P
							W
							-
							CTG
							CCA
							TGG
							TAG

Translation begun with base no. 57

Translated to base no. 995

Sequence printed from base no. 57 to base no. 995

Sequence numbered beginning with base no. 57

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Figure 16A Translated sequence of I9T.D1S

10	20	30	40	50	60
* ATG ACT AGA AGA AAC CAA ACT GCC ATC TCT CAG TTC TTC CTT CTG GGC CTG CCA TTC CCC M T R R N Q T A I S Q F F L L G L P F P	* 70	* 80	* 90	* 100	* 110
* CCA GAG TAC CAA CAC CTG TTC TAT GCC CTG TTC CTG GGC ATG TAC CTC ACC ACT CTC CTC P E Y Q H L F Y A L F L A M Y L T T L L	* 130	* 140	* 150	* 160	* 170
* GGG AAC CTC ATC ATC ATC CTC ATT CTA CTG GAC TCC CAT CTC CAC ACA CCC ATG TAC G N L I I I I L L L D S H L L P M Y	* 190	* 200	* 210	* 220	* 230
* TTG TTT CTC AGC AAT TTA TCC TTT GCC GAC CTC TGT TTT TCC TCT GTC ACA ATG CCC AAG L F L S N L S F A D L C F S S V T M P K	* 250	* 260	* 270	* 280	* 290
					300

Figure 16B * * * * *
 TTG TTG CAG AAC ATG CAG AGC CAA GTT CCA TCC ATC CCC TAT GCA GGG TGC CTG GCA CAG *
 L L Q N M Q S Q S Q V P S I P Y A C C L A Q
 310 320 330 340 350 360
 * * * * *
 ATA TAC TTC TTT CTG TTT TTT GGA GAC CTT GGA AAC TTC CTG CTT GTG GCC ATG GCC TAT
 I Y F F L F F G D L L G N F L L V A M A Y
 370 380 390 400 410 420
 * * * * *
 GAC CGC TAT GTG GCC ATC TGC TTC CCC CTT CAT TAC ATG AGC ATC ATG AGC CCC AAG CTC
 D R Y V A I C F F P L L H Y M S I M S P K L
 430 440 450 460 470 480
 * * * * *
 TGT GTG AGT CTG GTG CTG TCC TGG GTG CTG ACT ACC TTC CAT GCC ATG CTG CAC ACC
 C V S L V V' L S S W V L T T F H A M L H T
 490 500 510 520 530 540
 * * * * *
 CTG CTC ATG GCC AGA TTG TCA TTC TGT GAG GAC AGT GTG ATC CCT CAC TAT TTC TGT GAT
 L L M A R L S F C E D S V I P H Y F C D
 550 560 570 580 590 600
 * * * * *
 ATG TCT ACT CTG CTG AAA GTG GCT TGT TCT GAC ACC CAT GAT AAT GAA TTA GCA ATA TTT
 M S T L L K V A C S D T H D N E L A I F

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Figure 16C

610	*	620	*	630	*	640	*	650	*	660	*
ATC TTA GGG GGC CCT ATA GTT GTA CTA CCT TTC CTT CTC ATC ATT GTT TCT TAT GCA AGA											
I L G G P I V V V L P F L L I I V S Y A R											
670	*	680	*	690	*	700	*	710	*	720	*
ATT GTT TCC TCC ATC TTC AAG GTC CCT TCT TCT CAA AGC ATC CAT AAA GCC TTC TCC ACC											
I V S S I F K V V P S S S Q S I H K A F S T											
730	*	740	*	750	*	760	*	770	*	780	*
TCT GGC TCC CAC CTG TCT GTG TCA CTG TTC TAT GGG ACA GTC ATT GGT CTC TAC TTA											
C G S H L S V V V S L F Y G T V I G L Y L											
790	*	800	*	810	*	820	*	830	*	840	*
TGT CCT TCA GCT AAT AAC TCC ACT GTG AAG GAG ACT GTC ATG TCT TTG ATG TAC ACA ATG											
PRONUC/TRA											
C P S A N N S T V K E T V M S L M Y T M											

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Figur 16D

850	*	860	*	870	*	880	*	890	*	900	*
GTG ACA CCC ATG CTG AAC CCC TTC ATC TAC AGC CTA AGA AAC AGA GAC ATA AAA GAT GCA											
V T P M L N P F I Y S L R N R D I K D A											
910	*	920	*	930	*	940	*				
TTA GAA AAA ATA ATG TGC AAA AAG CAA ATT CCC TCC TTT CTA TGA											
L E K I M C K K Q I P S F L -											

Translation begun with base no. 200

Translated to base no.1144

Sequence printed from base no. 200 to base no.1144

Sequence numbered beginning with base no. 200

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Figure 17A Translated sequence of 114T.D1S

10	20	30	40	50	60
* ATG ACT GGA AAT AAC CAA ACT TTG ATC TTC GAG TTC CTC CTG GGT CTG CCC ATC CCA M T G N N Q T L I L E F L L L G L P I P	* 20	* 30	* 40	* 50	* 60
70	80	90	100	110	120
* TCA GAG TAT CAT CTC CTG TTC TAT GCC CTG TTC CTG GCC ATG TAC CTC ACC ATC ATC CTG S E Y H L L F Y A L F L A M Y L T I I L	* 80	* 90	* 100	* 110	* 120
130	140	150	160	170	180
* GGA AAC CTG CTA ATC ATT GTC CTT GTT CGA CTG GAC TCT CAT CTC CAC ATG CCC ATG TAC G N L L I I V L V L R L D S H L L H M P M Y	* 140	* 150	* 160	* 170	* 180
190	200	210	220	230	240
* TTG TTT CTC ACC AAC TTG TCC TTC TCT GAC CTC TGC TGT TCC TCT GTC ACA ATG CCC AAA L F L S N L S F S D L C F S S V T M P K	* 200	* 210	* 220	* 230	* 240
250	260	270	280	290	300
* TTG CTT CAG AAC ATG CAG AGC CAA GTA CCA TCT ATA TCC TAT ACA GGC TGC CTG ACA CAG L L Q N M Q S S Q V P S I S Y T G C L T Q	* 260	* 270	* 280	* 290	* 300

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Figure 17B

310	320	330	340	350	360
* CTG TAC TTC TTT ATG GTT TTT GGA GAT ATG GAG AGC TTC CTT CTT GTG GTG ATG GCC TAT	* L Y F F M V F G D M E S F L L L V V M A Y	* 380	* 400	* 410	* 420
370	380	390	400	410	420
* GAC CGC TAT CTG GCC ATT TGC TTT CCT TTG CGT TAC ACC ACC ATC ATG AGC ACC AAG TTC	* D R Y V A I C F P L R Y T T I M S T K F	430	440	450	460
* TGT GCT TCA CTA GTG CTA CTT CTG TGG ATG CTG ACG ATG ACC CAT GCC CTG CTG CAT ACC	* C A S L V L L L L W M L T M T H A L L H T	490	500	510	520
* CTA CTC ATT GCT AGA TTG TCT TTT TGT GAG AAG AAT GTG ATT CTT CAC TTT TTC TGT GAC	* L L I A R L L S F C E K N V I L L H F F C D	550	560	570	580
* ATT TCT GCT CTT CTG AAG TTG TCC TGC TCA GAC ATT TAT GTT AAT GAG CTG ATG ATA TAT	* I S A L L L K L S C S D I Y V N E L M I Y	610	620	630	640
					650
					660

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Figure 17C

ATC	TTC	GGT	GGA	CTC	ATC	ATT	ATT	ATC	CCA	TTC	CTA	TTA	ATT	GTT	ATG	TCC	TAT	GTT	ACA	*
I	L	G	G	L	I	I	I	I	P	F	L	L	I	V	M	S	Y	V	R	*
670	*					680	*		690	*		700	*			710	*		720	*
ATT	TTC	TTC	TCC	ATT	TTG	AAG	TTT	CCA	TCT	ATT	CAG	GAC	ATC	TAC	AAG	GTA	TTC	TCA	ACC	*
I	F	F	S	I	L	K	F	P	S	I	Q	D	I	Y	K	V	F	S	T	*
730	*					740	*		750	*		760	*			770	*		780	*
TGT	GGT	TCC	CAT	CTG	TCT	GTG	GTG	ACC	TTG	TTT	TAT	GGG	ACA	ATT	TTT	GCT	ATC	TAC	TTA	*
C	G	S	H	L	S	V	V	T	L	F	Y	G	T	I	F	G	I	Y	L	*
790	*					800	*		810	*		820	*			830	*		840	*
TGT	CCA	TCA	GGT	AAT	AAT	TCT	ACT	GTG	AAG	GAG	ATT	GCC	ATG	GCT	ATG	ATG	TAC	ACA	CTG	*
PRONUC/TRA OPTION																				
C	P	S	G	N	N	S	T	V	K	E	I	A	M	A	M	M	Y	T	V	
850	*					860	*		870	*		880	*			890	*		900	*
CTG	ACT	CCC	ATG	CTG	AAT	CCC	TTT	ATC	TAC	AGC	CTG	AGG	AAC	ACA	GAC	ATG	AAA	AGG	GCC	*
V	T	P	M	L	N	P	F	I	Y	S	L	R	N	R	D	M	K	R	A	*

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Figure 17D

	910		920		930		9
	*		*		*		
CTA	ATA	AGA	GTT	ATC	TGC	ACT	AAG
L	I	R	V	I	C	T	K
							K
							I
							S
							L
							-
							TAA

Translation begun with base no. 64

Translated to base no.1002

Sequence printed from base no. 64 to base no.1002

Sequence numbered beginning with base no. 64

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65/98

Figure 18A Translated sequence of 115T.D1S

10	20	30	40	50	60
* ATG ACA GAA GAG AAC CAA ACT GTG ATC TCC CAG TTC CTT CTC CTT TTC CTG CCC ATC CCC	* M T E E N Q T V I S Q F L L L F L P I P	* 70	* 80	* 90	* 100
* TCA GAG CAC CAG CAC GTG TTC TAC GCC CTG TTC CTG TCC ATG ATG TAC CTC ACC ACT GTC CTG	* S E H Q H V F Y A L F L S M Y L T T V L	* 130	* 140	* 150	* 160
* GGG AAC CTC ATC ATC ATC CTC ATT CAC CTG GAC TCC CAT CTC CAC ACA CCC ATG TAC	* G N L I I I I L I H L D S H L H T P M Y	* 190	* 200	* 210	* 220
* TTG TTT CTC AGC AAC TTG TCC TTC TCT GAT CTC TGC TGC TTT TCC TCT TCT GTT ACG ATG CCC AAG	* L F L S N L S F S D L C F S S S V T M P K	* 250	* 260	* 270	* 280
* TTG TTG CAG AAC ATG CAG AGC CAA GTT CCA TCC ATC CCC TTT GCA GGC TGC CTG ACA CAA	* 300				

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Figure 18B

310	320	330	340	350	360
* TTA TAC TTT TAC CTG TAT TTT GCA GAC CTT GAG AGC TTC CTG CTT CTG GCC ATG GCC TAT	* L Y F Y L Y Y F A D L L E S F L L V A M A Y	* 330	* 340	* 350	* 360
370	380	390	400	410	420
* GAC CGC TAT GTG GCC ATC TGC TTC CCC CTT CAT TAC ATG AGC ATC ATG AGC CCC AAG CTC	* D R Y V A I C F P L L H Y M S I M S P K L	* 390	* 400	* 410	* 420
430	440	450	460	470	480
* TGT CTG AGT CTG GTG GTG CTG TCC TCG GTG CTG ACC ACC TTC CAT GCC ATG CTG CAC ACC	* C V S L L V V L S W V L T T F H A M L H T	* 450	* 460	* 470	* 480
490	500	510	520	530	540
* CTG CTC ATG GCC AGA TTG TCA TTC TGT GCG GAC AAT ATG ATC CCC CAC TTT TTC TGT GAT	* L L M A R L L S F C A D N M I P H F C D	* 510	* 520	* 530	* 540
550	560	570	580	590	600
* ATA TCT CCT TTA TTG AAA CTG TCC TCG TCT GAC ACC CAT GTT AAT GAG TTG GTG ATA TTT	* I S P L L L K L S C S D T H V N E L V I F	* 570	* 580	* 590	* 600
610	620	630	640	650	660

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Figure 25B

```
301  XXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXX+360
      ? ? ? ? ? ? ? ? ? ? ? ? ? ? ? ? ? ? ? ? ? ? ? ? -
361  XXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXX+420
      ? ? ? ? ? ? ? ? ? ? ? ? ? ? ? ? ? ? ? ? ? ? ? ? -
      ATTGTCGCATCCTCATCTTACATCTACATCACCAATGCAGTCTCAGAGTCTCATC+480
      P V C I L I S Y I Y I T N A V L R V S S -
481  CTTAGGGGAGGATGGAAAGCCTTCTCCACCTGTGGCTCACACCTGGCTGTGGTCTGCCCT+540
      F R G G W K A F S T C G S H L A V V C L
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Figure 25C

CTTCTATGGCACCACATCTGCTGTATTTCAATCCGTATCTTCCCATTCATCTGAGAA
541 -----+-----+-----+-----+-----+-----+600
F Y G T I I A V Y F N P V S S H S S E K -
GGACACTGCAGCAACTGTGCTATACACAGTGGTGACTCCCATGTTG
601 -----+-----+-----+-----+-----+-----646
D T A A T V L Y T V V T P M L -

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Figure 26A

J14

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1  TGCTGCTTCTCTCCACCACCTGTCCCAAGGTACTGGCTAACCACATACTCACTAGTCA
   -----+-----+-----+-----+-----+-----+-----+-----+
60  V C F S S T T V P K V L A N H I L S S Q -

61  GGCCATTCTCTGGCTGTCTAACTCAGCTGTATTTCTCTGTGTCTGTGAATAT
   -----+-----+-----+-----+-----+-----+-----+-----+
120  A I S F S G C L T Q L Y F L C V S V N M

121  GGACAAATTTCCTGCTGGCTGTGATGGCCTATGACAGATTGTGGCCCATATGCCACCCCTTT
   -----+-----+-----+-----+-----+-----+-----+-----+
180  D N F L L A V M A Y D R F V A I C H P L -

181  GTACTACACAACAAGATGACCCACCAGCTCTGTGCTGTGGTGTCTGGATCAXXXX
   -----+-----+-----+-----+-----+-----+-----+-----+
240  Y Y T T K M T H Q L C V L L V S G S ? ?

241  XXXXXX XXXXXX XXXXXX XXXXXX XXXXXX XXXXXX XXXXXX XXXXXX
   -----+-----+-----+-----+-----+-----+-----+-----+
300  ? ? ? ? ? ? ? ? ? ? ? ? ? ? ? ? ? ? ? ? ? ?

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Figure 26B

```

301  XXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXX+360
    ? ? ? ? ? ? ? ? ? ? ? ? ? ? ? ? ? ? ? ? ? ? ? ? ? ? ?
361  XXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXX+420
    ? ? ? ? ? ? ? ? ? ? ? ? ? ? ? ? ? ? ? ? ? ? ? ? ? ? ?
    ATTGTCGCATCCTCATCTCTTACATCTACATCACC AATGCAGTCCTCAGAGTCTCATC
421  F V C I L I S Y I Y I T N A V L R V S S -+480
    CTTTAGGGAGGATGGAAAGCCTTCTCCACCTGGCTCAGCTGCTGCTGCTGCTGCT
481  F R G G W K A F S T C G S H L A V V C L -+540
    CTTCTATGGCACCATCATGCTGTGTATTTCAATCCTGTATCTTCCCATTCATCTGAGAA
541  F Y C T I I A V Y P N P V S S H S S E K -+600
    GGACACTGCAGCAACTGTGCTATACACAGTGGTGA CTCCCATCTGTC
601  D T A A T V L Y T V V T P M L - 646

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Figure 27A

J15

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1  TATCTGCAACCCCTCTGCGGTACCCAGTCTCTCATGACCGCCGCGGTGCTCCTCATGCT
   -----+-----+-----+-----+-----+-----+-----+
   I C N P L R Y P V L M S G R V C L L M V 60
61  CGTGGCCCTCCTGGTTGGGAGGATCCCTCAACGCCCTCCATTTCAGACTTCTCTGACCCCTTCA
   -----+-----+-----+-----+-----+-----+-----+
   V A S W L G G S L N A S I Q T S L T L Q - 120
121 GTTCCCTACTGTGGATCACGGAGATCTCCCACTTCTTCTGTGAGGTGCCCTCGCTGCT
   -----+-----+-----+-----+-----+-----+-----+
   F P Y C G S R K I S H F P C E V P S L L - 180
181 GAXXXTGGCCCTGTGCAGACACTGAAGCCCTATGAGCAGGTACTATTGTGACAGGCGTGGT
   -----+-----+-----+-----+-----+-----+-----+
   ? ? A C A D T E A Y E Q V L F V T G V V - 240

```

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Figure 27B

GGTCCTCCTGGTGCCCATTCATTACTGCCTCTTATGCCCTCATCCTGGCTGCTGT
-----+-----+-----+-----+-----+
241 V L L V P I T P I T A S Y A L I L A A V
GCTCCGAATGCACCTCTGGGAGGGAGTCAGAAGCCCTAGCCACATGCTCCTCTCACCT
-----+-----+-----+-----+-----+360
301 L R M H S A E G S Q K A L A T C S S H L -
GACAGTCGTCAATCTTCTATGGGCCCTTGCTACACCTACATGTTACCTGCTTCCTA
-----+-----+-----+-----+-----+420
361 T V V N L F Y G P L V Y T Y M L P A S Y -
TCACTCACCAGGCCAAGACGACATAGTATCCGCTCTTTACACCGTCTCACCACCATGCT
-----+-----+-----+-----+-----+480
421 H S P G Q D D I V S V F Y T V L T P M L -

T
481 - 481
A

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Figure 28A

J16

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CATCTGTAGGCTCTTCACTATCTCTACCTCATGACCCAGACACTGTGTGCCAAGATTGC
1  -----+-----+-----+-----+-----+-----+ 50
   I C R P L H Y P T L M T Q T L C A K I A -
   CACTGGTTCGCTTGGGAGGCTTGGCTGGGCCAGTGGTAGAAATTTCCTTGGTCTCTCG
61 -----+-----+-----+-----+-----+-----+ 120
   T G C W L G G L A G P V V E I S L V S R -
   TCTCCTTTTGTGGCCCAATCACATTCACACATCTTTTGTGATTTCCACCTGTGCT
121 -----+-----+-----+-----+-----+-----+ 180
   L L F C G P N H I Q H I F C D F P P V L -
   GAGCTTGGCTTGTAATACATCAGTGAATGTCCTGGTAGATTTTATATAAACCTCTC
181 -----+-----+-----+-----+-----+-----+ 240
   S L A C T D T S V N V L V D F I I N L C -
   CAAGATCCTGGCCACCTTCCTGCTGATCCTGAGCTCCTACTTGCAGATAATCCGCACAGT
241 -----+-----+-----+-----+-----+-----+ 300
   K I L A T F L L I L S S Y L Q I I R T V -

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Figure 28B

181 GAGCTTGGCTTGTAACATCAGTGAATGCTCCTGGTAGATTTTATATAAACCTCTG
S L A C T D T S V N V L V D P I I N L C - +240 -

241 CAAGATCCTGGCCACCTTCCTGCTGATCCTGAGCTCCTACTTGCAGATAATCCGCACAGT
R I L A T F L L I L S S Y L Q I I R T V - +300 -

301 GCTCAAGATTCTCAGCTGCAGGCAGGAAGCAATCTCGACTTGTGCTCCCATCT
L K I P S A A G K K A P S T C A S H L - +360 -

361 CACTGTGGTTCTCATCTTCTATGGAGCATCCTTTTCATGTATGTGCGGCTGANGAAGAC
T V V L I F Y G S I L P M Y V R L K K S - +420 -

421 TTACTCCCTTGACTACGACAGAGCCTTGGCAGTAGTCTACTCCGTGGTTACCCCTTTCTCT
Y S L D Y D R A L A V V Y S V V T P F L - +480 -

93/99

Figure 29A

J17

```

1  AATCTOCAAACCCACTGCTTTATTCCACCAGAAATGICCCACACAGTCTGTATCCAGTTGGT
   I C N P L L Y S T K M S T Q V C I Q L V -
61  TGCAGGATCTATAGGGGTTTCTTAATACTGCCCTCATCATGTTTACTTTTCTC
   A G S Y I G G P L N T C L I M F Y F F S -
121 TTTTCTCTCTGTCGGCCAAATATAGTTGATCATTTTCTCTGTGATTTTGGCTCCTTTXXT
   F L P C G P N I V D H F F C D F A P ? ? -
181 GGAACTTTCGTCCTGATGTGAGTCTCTGTAGTGTGTATGTCATTTTCTGCTGGCTC
   E L S C S D V S V S V V M S F S A G S -
241 AGTTACTATGATCACAGTGTATTATCATAGCCATCTCCTATTCTTACATCCTCATCACCAT
   V T M I T V F I I A I S Y S Y I L I T I -
300
```

SUBSTITUTE SHEET

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Figure 29B

301 CCTGAAGATGTCCTCACTGAGCGCCGTCACAGGCTTTCTCCACATGTACCTCCACCT
-----+-----+-----+-----+-----+-----+360
L K M S S T B G R H K A F S T C T S H L -

361 CACTGCAGTCACCTCTACTATGGCACCATTACCTTTCATTTATGTATGCCCAAGTCCAC
-----+-----+-----+-----+-----+-----+420
T A V T L Y Y C T I T F I Y V M P K S T -

421 ATACTCTACAGACCAGAACAGGTGCTGTCTGTTTACATGCTGGTGATCCCAATGTT
-----+-----+-----+-----+-----+-----+480
Y S T D Q N K V V S V F Y M V V I P M L -

G
481 - 481

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Figure 30A

J19

```

1  TATCTGCCACCCCTCTGAAGTACACAGTTATCATGAATCACTATTTTGTGTGATGCTGCT
   -----+-----+-----+-----+-----+-----+-----+-----+
   I C H P L K Y T V I M N H Y F C V M L L - 60
61  GCTCTTCTCTGTTCTGTTAGCACTGCACATGCTTCTTCCACATTTTAAATGGTGTGAT
   -----+-----+-----+-----+-----+-----+-----+-----+
   L F S V F V S I A H A L F H I L M V L I - 120
121 ACTGACTTTCAGCACAAAACCTGAATCCCTCAGCTTTTCTGTGAGCTGGCTCATATCAT
   -----+-----+-----+-----+-----+-----+-----+-----+
   L T F S T K T E I P H F F C E L A H I I - 180
181 CAAACTTACCCTGTTCCGATAATTTTATCAACTATCTGCTGATATACACAGAGTCTGTCTT
   -----+-----+-----+-----+-----+-----+-----+-----+
   K L T C S D N F I N Y L L I Y T E S V L - 240
241 ATTTTGTGTTCATATTGTAGGATCATTTTGTCTTATATTACACGTATCCCTCAGT
   -----+-----+-----+-----+-----+-----+-----+-----+
   F F G V H I V G I I L S Y I Y T V S S V - 300

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Figure 30B

```
301  TTTAAGAAATGTCATTATGGGAGGAATGTATAAGCCCTTTTCACATGTGGATCTCATTT
      L R M S L L G G M Y K A F S T C G S H L - +360
361  GTCGGTGTCCTCTGTTTATGGCACAGGTTTTCGGGTACACATAAGCTCTCCACTTACTG
      S V V S V L W H R F W G T H K L S T Y * +420
421  ACCTCCAAGGAAGACCTGTAGTGGCTTCAGTGTATGTACACTGTGGTTACTCAGATGCTG
      L S K E D C S G F S D V H C G Y S D A - 479
```

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Figure 31A

```

1  AATCTGCTACCCACTGAGGTACCTTCTCATCATGAGCTGGTGGTGTGCACAGCACTGTC
   -----+-----+-----+-----+-----+-----+-----+
60  I C Y P L R Y L L I M S W V V C T A L S -
   -----+-----+-----+-----+-----+-----+-----+

61  CGTGGCAATCTGGGTCATAGGCTTTTGTGCTCCTCCGTTATACCTCTCTGCTTCACGATCCT
   -----+-----+-----+-----+-----+-----+-----+
120  V A I W V I G F C A S V I P L C F T I L -
   -----+-----+-----+-----+-----+-----+-----+

121  CCCACTCTGTGGTCCCTTACGTGCTGATTATCTTTTCTGGGAGCTGCCCATCTTCTTGCA
   -----+-----+-----+-----+-----+-----+-----+
180  P L C G P Y V V D Y L F C E L P I L L H -
   -----+-----+-----+-----+-----+-----+-----+

181  CCTGTTCTGCACAGATACATCTCTGCTGGAGXXXXXXXXXXXXXX
   -----+-----+-----+-----+-----+-----+-----+
240  L F C T D T S L L E ? ? ? ? ? ? ? ? ? ? -
   -----+-----+-----+-----+-----+-----+-----+

241  XXXXXXXXXXXXXCCCTTCTCTGATGTCTCTCTACCTTGGCATCTGGTGGCTGTG
   -----+-----+-----+-----+-----+-----+-----+
300  ? ? ? ? P F L L I V L S Y L R I L V A V
   -----+-----+-----+-----+-----+-----+-----+

```

J20

SUBSTITUTE SHEET

Figure 31B

301 ATAAGAATAGACTCAGCTGAGGGCAGAAAAAGGCCCTTTTCAACTTGTGCTTCACACTTG
 -----+-----+-----+-----+-----+-----+-----+360
 I R I D S A E G R K K A F S T C A S H L

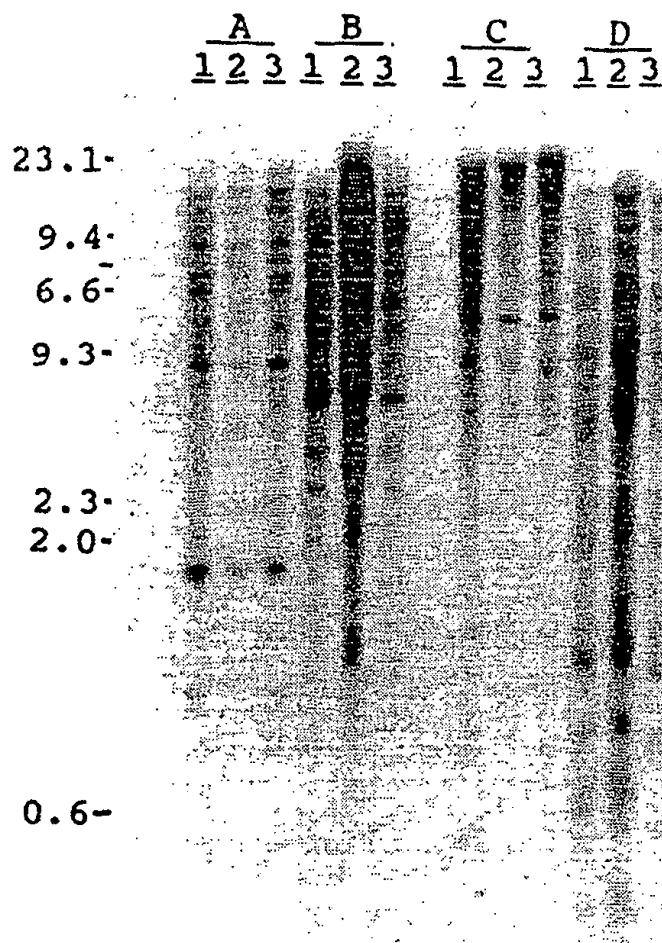
361 GCTGTGCTGACCATCTACTATGGACAGGGCTGATCAGGTACTTGAGGCCCAAGTCCCTT
 -----+-----+-----+-----+-----+-----+-----+420
 A V V T I Y Y G T G L I R Y L R P K S L

421 TATTCCGCTGAGGGAGACAGACTGATCTCTGTGTTCTATGCAGTCATTGGCCCTGCAC TG
 -----+-----+-----+-----+-----+-----+-----+480
 Y S A E G D R L I S V F Y A V I G P A L

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Figure 32

SUBSTITUTE SHEET

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US92/02741

A. CLASSIFICATION OF SUBJECT MATTER

IPC(5) : C12N 15/12, 15/63, 15/64, 5/10; C07K 13/00; A01N 33/00; A61K 37/00
US CL : 536/27; 424/418; 435/7.21, 172.3, 240.1, 320.1; 514/2; 530/395
According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

U.S. : 536/27; 424/418; 435/7.21, 172.3 240.1, 320.1; 514/2; 530/395

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

CAS ONLINE, MEDLINE, UEMBL, GENBANK, PIR, SWISS PROT, APS

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
<u>X,P</u> <u>Y,P</u>	Molecular Brain Research, Volume 13, No. 1-2, issued March 1992, L. A. Selbie et al., "Novel G protein-coupled receptors: a gene family of putative human olfactory receptor sequences," abstract.	<u>1-32</u> <u>33-98</u>
<u>Y</u> <u>X</u>	Sensory Syst., Volume 1, No. 1, issued 1987, V. I. Novoselov et al., "The properties of receptor molecules from rat olfactory epithelium," abstract.	<u>1-34, 65-98</u> <u>35-64</u>
<u>X,P</u> <u>Y,P</u>	Nature, Volume 355, issued 30 January 1992, M. Parmentier et al., "Expression of members of the putative olfactory receptor gene family in mammalian germ cells," pages 453-455, see entire document.	<u>1-32</u> <u>33-98</u>
<u>Y</u> <u>X</u>	Biochimica Biophysica Acta, Volume 839, No. 3, issued 1985, E. E. Fesenko et al., "Molecular mechanisms of olfactory reception. VI Kinetic characteristics of camphor interaction with binding sites of rat olfactory epithelium," abstract.	<u>1-34, 65-98</u> <u>35-64</u>

☒ Further documents are listed in the continuation of Box C. ☐ See patent family annex.

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Date of the actual completion of the international search

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Date of mailing of the international search report

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INTERNATIONAL SEARCH REPORT

International application No.
PCT/US92/02741

C (Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X,P Y,P	Chemtracts: Organic Chemistry, Volume 4, No. 4, issued 1991, K. Touhara et al., "A novel multigene family may encode odorant receptors: a molecular basis for odor recognition," abstract.	1-32 33-98
Y,P	Chemical Senses, Volume 16, No. 5, issued 1991, R. H. R. Anholt, "Odor recognition and olfactory transduction: the new frontier," abstract.	1-98
Y	Trends in Neuroscience, Volume 14, No. 7, issued 1991, S. Firestein, "A noseful of odor receptors," abstract.	1-98
Y	Proceedings of the National Academy of Sciences, Volume 86, issued November 1989, E. Dancigier et al., "Olfactory marker protein gene: Its structure and olfactory neuron-specific expression in transgenic mice," pages 8565-8569, see entire document.	1-34
Y	Kagaky Kogyo, Volume 40, No. 11, issued 1989, M. Kashiwayanagi et al., "High sensitivity odor sensor using artificial membrane," abstract.	1-98

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INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(51) International Patent Classification ⁵ : C12N 15/12, 15/63, 15/64 C12N 5/10, C07K 13/00 A01N 33/00, A61K 37/00	A1	(11) International Publication Number: WO 92/17585 (43) International Publication Date: 15 October 1992 (15.10.92)
(21) International Application Number: PCT/US92/02741 (22) International Filing Date: 6 April 1992 (06.04.92) (30) Priority data: 681,880 5 April 1991 (05.04.91) US (60) Parent Application or Grant (63) Related by Continuation US 681,880 (CIP) Filed on 5 April 1991 (05.04.91) (71) Applicant (for all designated States except US): THE TRUSTEES OF COLUMBIA UNIVERSITY IN THE CITY OF NEW YORK [US/US]; Broadway and West 116th Street, New York, NY 10027 (US).	(72) Inventors; and (75) Inventors/Applicants (for US only): BUCK, Linda, B. [US/US]; 100 Haven Avenue, New York, NY 10032 (US). AXEL, Richard [US/US]; 445 Riverside Drive, New York, NY 10027 (US). (74) Agent: WHITE, John, P.; Cooper & Dunham, 30 Rockefeller Plaza, New York, NY 10112 (US). (81) Designated States: AT (European patent), AU, BE (European patent), CA, CH (European patent), DE (European patent), DK (European patent), ES (European patent), FR (European patent), GB (European patent), GR (European patent), IT (European patent), JP, LU (European patent), MC (European patent), NL (European patent), SE (European patent), US. Published <i>With international search report.</i>	
(54) Title: ODORANT RECEPTORS AND USES THEREOF (57) Abstract <p>The invention provides an isolated nucleic acid, e.g. cDNA encoding an odorant receptor. The invention further provides expression vectors containing such nucleic acid. Also provided is a purified protein encoding an odorant receptor, with the aforementioned expression vectors and the resulting transformed cell. The invention also provides methods of identifying odorant ligands and of identifying odorant receptors. The invention further provides methods of developing fragrances, of identifying appetite suppressant compounds, of controlling appetite, of controlling pest populations, of promoting and inhibiting fertility, and of detecting odors.</p>		

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ODORANT RECEPTORS AND USES THEREOF**Background of the Invention**

5 This application is a continuation-in-part of U.S. Serial No.681,880, filed April 5, 1991, the contents of which are hereby incorporated by reference.

10 Throughout this application, various publications are referenced by Arabic numerals within parentheses. Full citations for these publications may be found at the end of the specification immediately preceding the claims. The disclosures of these publications in their entireties are hereby incorporated by reference into this application in
15 order to more fully describe the state of the art as known to those skilled therein as of the date of the invention described and claimed herein.

20 In vertebrate sensory systems, peripheral neurons respond to environmental stimuli and transmit these signals to higher sensory centers in the brain where they are processed to allow the discrimination of complex sensory information. The delineation of the peripheral mechanisms by which environmental stimuli are transduced into neural information
25 can provide insight into the logic underlying sensory processing. Our understanding of color vision, for example, emerged only after the observation that the discrimination of hue results from the blending of information from only three classes of photoreceptors (1, 2, 3, 4). The basic
30 logic underlying olfactory sensory perception, however, has remained elusive. Mammals possess an olfactory system of enormous discriminatory power (5, 6). Humans, for example, are thought to be capable of distinguishing among thousands of distinct odors. The specificity of odor recognition is
35 emphasized by the observation that subtle alterations in the molecular structure of an odorant can lead to profound

-2-

changes in perceived odor.

The detection of chemically distinct odorant presumably results from the association of odorous ligands with specific receptors on olfactory neurons which reside in a specialized epithelium in the nose. Since these receptors have not been identified, it has been difficult to determine how odor discrimination might be achieved. It is possible that olfaction, by analogy with color vision, involves only a few odor receptors, each capable of interaction with multiple odorant molecules. Alternatively, the sense of smell may involve a large number of distinct receptors each capable of associating with one or a small number of odorant. In either case, the brain must distinguish which receptors or which neurons have been activated to allow the discrimination between different odorant stimuli. Insight into the mechanisms underlying olfactory perception is likely to depend upon the isolation of the odorant receptors, and the characterization of their diversity, specificity, and patterns of expression.

The primary events in odor detection occur in a specialized olfactory neuroepithelium located in the posterior recesses of the nasal cavity. Three cell types dominate this epithelium (Figure 1A): the olfactory sensory neuron, the sustentacular or supporting cell, and the basal cell which is a stem cell that generates olfactory neurons throughout life (7, 8). The olfactory sensory neuron is bipolar: a dendritic process extends to the mucosal surface where it gives rise to a number of specialized cilia which provide an extensive, receptive surface for the interaction of odors with olfactory sensory neurons. The olfactory neuron also gives rise to an axon which projects to the olfactory bulb of the brain, the first relay in the olfactory system. The axons of the olfactory bulb neurons, in turn, project to

-3-

subcortical and cortical regions where higher level processing of olfactory information allows the discrimination of odors by the brain.

5 The initial events in odor discrimination are thought to involve the association of odors with specific receptors on the cilia of olfactory neurons. Selective removal of the cilia results in the loss of olfactory response (9).
10 Moreover, in fish, whose olfactory system senses amino acids as odors, the specific binding of amino acids to isolated cilia has been demonstrated (10, 11). The cilia are also the site of olfactory signal transduction. Exposure of isolated cilia from rat olfactory epithelium to numerous odorant leads to the rapid stimulation of adenylyl cyclase
15 and elevations in cyclic AMP (an elevation in IP3 in response to one odorant has also been observed) (12, 13, 14, 15). The activation of adenylyl cyclase is dependent on the presence of GTP and is therefore likely to be mediated by receptor-coupled GTP binding proteins (G-proteins) (16).
20 Elevations in cyclic AMP, in turn, are thought to elicit depolarization of olfactory neurons by direct activation of a cyclic nucleotide-gated, cation permeable channel (17, 18). This channel is opened upon binding of cyclic nucleotides to its cytoplasmic domain, and can therefore
25 transduce changes in intracellular levels of cyclic AMP into alterations in the membrane potential.

These observations suggest a pathway for olfactory signal transduction (Figure 1B) in which the binding of odors to
30 specific surface receptors activates specific G-proteins. The G-proteins then initiate a cascade of intracellular signalling events leading to the generation of an action potential which is propagated along the olfactory sensory axon to the brain. A number of neurotransmitter and hormone
35 receptors which transduce intracellular signals by

-4-

activation of specific G-proteins have been identified. Gene cloning has demonstrated that each of these receptors is a member of a large superfamily of surface receptors which traverse the membrane seven times (19, 20). The
5 pathway of olfactory signal transduction (Figure 1B) predicts that the odorant receptors might also be members of this superfamily of receptor proteins. The detection of odors in the periphery is therefore likely to involve signalling mechanisms shared by other hormone or
10 neurotransmitter systems, but the vast discriminatory power of the olfactory system will require higher order neural processing to permit the perception of individual odors. This invention address the problem of olfactory perception at a molecular level. Eighteen different members of an
15 extremely large multigene family have been cloned and characterized which encodes seven transmembrane domain proteins whose expression is restricted to the olfactory epithelium. The members of this novel gene family encode the individual odorant receptors.

20

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SUMMARY OF THE INVENTION

The invention provides an isolated nucleic acid, e.g. a DNA and cDNA molecule, encoding an odorant receptor. The invention further provides expression vectors containing such nucleic acid. Also provided by the invention is a purified protein encoding an odorant receptor. The invention further provides a method of transforming cells which comprises transfecting a suitable host cell with a suitable expression vector containing the nucleic acid encoding the odorant receptor.

The invention also provides methods of identifying odorant ligands and of identifying odorant receptors. The invention further provides methods of developing fragrances, of identifying appetite suppressant compounds, of controlling appetite. The invention also provides methods of controlling insect and other animal populations. The invention additionally provides a method of detecting odors such as the vapors emanating from Cocaine, Marijuana, Heroin, Hashish, Angel Dust, gasoline, decayed human flesh, alcohol, gun powder explosives, plastic explosives, firearms, poisonous or harmful smoke, or natural gas.

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Description of the Figures

Figure 1. The Olfactory Neuroepithelium and a Pathway for Olfactory Signal Transduction. A. The Olfactory Neuroepithelium. The initial event in odor perception occurs in the nasal cavity in a specialized neuroepithelium which is diagrammed here. Odors are believed to interact with specific receptors on the cilia of olfactory sensory neurons. The signal generated by these initial binding events are propagated by olfactory neuron axons to the olfactory bulb. B. A Pathway of Olfactory Signal Transduction. In this scheme, the binding of an odorant molecule to an odor-specific transmembrane receptor leads to the interaction of the receptor with a GTP-binding protein ($G_{S[olf]}$). This interaction, in turn, leads to the release of the GTP-coupled α -subunit of the G-protein, which then stimulates adenylyl cyclase to produce elevated levels of cAMP. The increase in cAMP opens nucleotide-gated cation channels, thus causing an alteration in membrane potential.

20

Figure 2. A PCR Amplification Product Containing Multiple Species of DNA. cDNA prepared from olfactory epithelium RNA was subjected to PCR amplification with a series of different primer oligonucleotides and the DNA products of appropriate size were isolated, further amplified by PCR, and size fractionated on agarose gels (A) (For details, see text). Each of these semipurified PCR products was digested with the restriction enzyme, Hinf I, and analyzed by agarose gel electrophoresis. Lanes marked "M" contain size markers of 23.1, 9.4, 5.6, 4.4, 2.3, 2.0, 1.35, 1.08, 0.87, 0.60, 0.31, 0.28, 0.23, 0.19, 0.12 and 0.07kb. (B). Twenty-two of the 64 PCR products that were isolated and digested with Hinf I are shown here. Digestion of one of these, PCR 13, yielded a large number of fragments whose sizes summed to a value much greater than that of the undigested PCR 13

35

-7-

DNA, indicating that PCR 13 might contain multiple species of DNA which are representatives of a multigene family.

Figure 3. Northern Blot Analysis with a Mixture of Twenty Probes. One μ g of polyA⁺ RNA isolated from rat olfactory epithelium, brain, or spleen was size-fractionated in formaldehyde agarose, blotted onto a nylon membrane, and hybridized with a ³²P-labeled mixture of segments of 20 cDNA clones. The DNA segments were obtained by PCR using primers homologous to transmembrane domains 2 and 7.

Figure 4. The Protein Sequences Encoded by Ten Divergent cDNA Clones. Ten divergent cDNA clones were subjected to DNA sequence analyses and the protein sequence encoded by each was determined. Amino acid residues which are conserved in 60% or more of the proteins are shaded. The presence of seven hydrophobic domains (I-VII), as well as short conserved motifs shared with other members of the superfamily, demonstrate that these proteins belong to the seven transmembrane domain protein superfamily. Motifs conserved among members of the superfamily and the family of olfactory proteins include the GN in TM1 (transmembrane domain 1), the central W of TM4, the Y near the C-terminal end of TM5, and the NP in TM7. In addition, the DRY motif C-terminal to TM3 is common to many members of the G-protein-coupled superfamily. However, all of the proteins shown here share sequence motifs not found in other members of this superfamily and are clearly members of a novel family of proteins.

Figure 5. Positions of Greatest Variability in the Olfactory Protein Family. In this diagram, the protein encoded by cDNA clone I15 is shown traversing the plasma membrane seven times with its N-terminus located extracellularly, and its C-terminus intracellularly. The

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vertical cylinders delineate the seven putative α -helices spanning the membrane. Positions at which 60% or more of the 10 clones shown in Figure 4 share the same residue as I15 are shown as white balls. More variable residues are shown as black balls. The high degree of variability encountered in transmembrane domains III, IV, and V is evident in this schematic.

Figure 6. The Presence of Subfamilies in a Divergent Multigene Family. Partial nucleotide sequences and deduced protein sequences were obtained for 18 different cDNA clones. Transmembrane domain V along with the flanking loop sequences, including the entire cytoplasmic loop between transmembrane domains V and VI, are shown here for each protein. Amino acid residues found in 60% or more of the clones in a given position are shaded (A). This region of the olfactory proteins (particularly transmembrane domain V) appears to be highly variable (see Figure 4). These proteins, however, can be grouped into subfamilies (B,C,D) in which the individual subfamily members share considerable homology in this divergent region of the protein.

Figure 7. Southern Blot Analyses with Non-crosshybridizing Fragments of Divergent cDNAs. Five μ g of rat liver DNA was digested with Eco RI (A) or Hind III (B), electrophoresed in 0.75% agarose, blotted onto a nylon membrane, and hybridized to the 32 P-labeled probes indicated. The probes used were PCR-generated fragments of: 1, clone F9 (identical to F12 in Figure 4); 2, F5; 3, F6; 4, I3; 5, I7; 6, I14; or 7, I15. The lane labeled "1-7" was hybridized to a mixture of the seven probes. The probes used showed either no crosshybridization or only trace crosshybridization with one another. The size markers on the left correspond to the four blots on the left (1-4) whereas the marker positions noted on the right correspond to the four blots on the right

-9-

(5-7, "1-7").

- Figure 8. Northern Blot Analysis with a Mix of Seven Divergent Clones. One μg of polyA⁺ RNA from each of the tissues shown was size-fractionated, blotted onto a nylon membrane, and hybridized with a ³²P-labeled mixture of segments of seven divergent cDNA clones (see Legend to Figure 7).
- Figure 9. The amino acid and nucleic acid sequence of clone F3.
- Figure 10. The amino acid and nucleic acid sequence of clone F5.
- Figure 11. The amino acid and nucleic acid sequence of clone F6.
- Figure 12. The amino acid and nucleic acid sequence of clone F12.
- Figure 13. The amino acid and nucleic acid sequence of clone I3.
- Figure 14. The amino acid and nucleic acid sequence of clone I7.
- Figure 15. The amino acid and nucleic acid sequence of clone I8.
- Figure 16. The amino acid and nucleic acid sequence of clone I9.
- Figure 17. The amino acid and nucleic acid sequence of clone I14.

-10-

Figure 18. The amino acid and nucleic acid sequence of clone I15.

5 Figure 19. The amino acid and nucleic acid sequence of human clone H5.

10 Figure 20. The amino acid and nucleic acid sequence of clone J1, where the reading frame starts at nucleotide position 2.

Figure 21. The amino acid and nucleic acid sequence of clone J2.

15 Figure 22. The amino acid and nucleic acid sequence of clone J4, where the reading frame starts at nucleotide position 2.

20 Figure 23. The amino acid and nucleic acid sequence of clone J7, where the reading frame starts at nucleotide position 2.

25 Figure 24. The amino acid and nucleic acid sequence of clone J8, where the reading frame starts at nucleotide position 2.

Figure 25. The amino acid and nucleic acid sequence of clone J11.

30 Figure 26. The amino acid and nucleic acid sequence of clone J14, where the reading frame starts at nucleotide position 2.

35 Figure 27. The amino acid and nucleic acid sequence of clone J15, where the reading frame starts at nucleotide position 2.

-11-

Figure 28. The amino acid and nucleic acid sequence of clone J16, where the reading frame starts at nucleotide position 2.

5 Figure 29. The amino acid and nucleic acid sequence of clone J17, where the reading frame starts at nucleotide position 2.

10 Figure 30. The amino acid and nucleic acid sequence of clone J19, where the reading frame starts at nucleotide position 2.

15 Figure 31. The amino acid and nucleic acid sequence of clone J20, where the reading frame starts at nucleotide position 2.

20 Figure 32. SOUTHERN BLOT: Five micrograms of DNA isolated from 1. Human placenta, 2. NCI-H-1011 neuroblastoma cells, or 3. CHP 134 neuroblastoma cells were treated with the restriction enzyme A. Eco RI, B. Hind III, C. Bam HI, or D. Pst I, and then electrophoresed on an agarose gel and blotted onto a nylon membrane. The blotted DNA was hybridized to the 32P-labeled H3/H5 sequence. An autoradiograph of the hybridized blot is shown with the
25 sizes of co-electrophoresed size markers noted in kilobases.

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Detailed Description of the Invention

The invention provides an isolated nucleic acid, e.g. a DNA or cDNA molecule, encoding an odorant receptor. Such a
5 receptor is a receptor which binds an odorant ligand and include but not limited to pheromone receptors. An odorant ligand may include, but is not limited to, molecules which interact with the olfactory sensory neuron, molecules which interact with the olfactory cilia, pheromones, and molecules
10 which interact with structures within the vomeronasal organ.

The invention specifically provides the isolated cDNAs encoding odorant receptors the sequences of which are shown in Figures 9-31. The nucleic acid is most typically a cDNA
15 and encodes an insect, a vertebrate, a fish or a mammalian odorant receptor. The mammalian odorant receptor is preferably a human, rat, mouse or dog receptor. In an embodiment, human odorant receptor cDNA sequence and the correspondent protein is isolated (Figure 19).

20 In another embodiment, pheromone receptors are isolated and shown as clones J1, J2, J4, J7, J8, J11, J14, J15, J16, J17, J19 and J20 (Figures 20-31).

25 The invention further provides expression vectors containing cDNA which encodes odorant receptors. Such expression vectors are well known in the art and include in addition to the nucleic acid the elements necessary for replication and expression in a suitable hosts. Suitable hosts are well
30 known in the art and include without limitation bacterial hosts such as E. coli, animal hosts such as CHO cells, insect cells, yeast cells and like.

The invention also provides purified proteins encoding
35 odorant receptors. Such proteins may be prepared by

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expression of the forementioned expression vectors in suitable host cells and recovery and purification of the receptors using methods well known in the art. Examples of such proteins include those having the amino acid sequences shown in figures 9-31.

The purified protein typically encodes an insect, vertebrate, fish or mammalian odorant receptor. The mammalian odorant receptor may be a human, rat, mouse or dog.

In one embodiment the invention provides a novel purified protein which belong to a class of proteins which have 7 transmembrane regions and a third cytoplasmic loop from the N-terminus which is approximately 17 amino acid long and to nucleic acid molecules encoding such proteins.

The invention provides methods of transforming cells which comprises transfecting a suitable host cell with a suitable expression vector containing nucleic acid encoding of the odorant receptor. Techniques for carrying out such transformations on cells are well known to those skilled in the art. (41,42) Additionally, the resulting transformed cells are also provided by the invention. These transformed cells may be either olfactory cells or non-olfactory cells. One advantage of using transformed non-olfactory cells is that the desired odorant receptor will be the only odorant receptor expressed on the cell's surface.

In order to obtain cell lines that express a single receptor type, standard procedures may be used to clone individual cDNAs or genes into expression vectors and then transfect the cloned sequences into mammalian cell lines. This approach has been used with sequences encoding some other members of the seven transmembrane domain superfamily

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including the 5HT_{1c} serotonin receptor. (43) The cited work illustrates how members of this superfamily transferred into cell lines may generate immortal cell lines that express high levels of the transfected receptor on the cell surface where it will bind ligand and that such abnormally expressed receptor molecules can transduce signals upon binding to ligand.

The invention also provides a method of identifying a desired odorant ligand which comprises contacting transformed non-olfactory cells expressing a known odorant receptor with a series of odorant ligands to determining which ligands bind to the receptors present on the non-olfactory cells.

Additionally, the invention provides a method of identifying a desired odorant receptor comprising contacting a series of transformed non-olfactory cells with a known odorant ligand and determining which odorant receptor binds with the odorant ligand.

The invention provides a method of detecting an odor which comprises: a) identifying a odorant receptor which binds the desired odorant ligand and; b) imbedding the receptor in a membrane such that when the odorant ligand binds to the receptor so identified a detectable signal is produced. In one embodiment of the invention the membrane used in this method is cellular, including a membrane of an olfactory cell or a synthetic membrane.

The ligand tested for may be the vapors emanating from Cocaine, Marijuana, Heroin, Hashish, Angel Dust, gasoline, decayed human flesh, alcohol, gun powder explosives, plastic explosives or firearms. In another embodiment the ligand tested for may be natural gas, a pheromone, toxic fumes,

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noxious fumes or dangerous fumes.

In one embodiment of the invention the detectable signal is a lightbulb lighting up, a buzzer buzzing, a bell ringing,
5 a color change, phosphorescence, or radioactivity.

The invention further provides a method of quantifying the amount of an odorant ligand present in a sample which comprises utilizing the above-mentioned method for odor
10 detection and then quantifying the amount of signal produced.

The invention further provides a method of developing fragrances which comprises identifying a desired odorant
15 receptor by the above method, then contacting non-olfactory cells, which have been transfected with an expression vector containing nucleic acid encoding the desired odorant receptor such that the receptor is expressed upon the surface of the non-olfactory cell, with a series of
20 compounds to determine which compound or compounds bind the receptor.

The invention provides to a method of identifying an "odorant fingerprint" which comprises contacting a series of
25 cells, which have been transformed such that each express a known odorant receptor, with a desired sample and determining the type and quantity of the odorant ligands present in the sample.

30 The invention provides a method of identifying odorant ligands which inhibit the activity of a desired odorant receptor which comprises contacting the desired odorant receptor with a series of compounds and determining which compounds inhibit the odorant ligand - odorant receptor
35 interaction.

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The invention also provides for a method of identifying appetite suppressant compounds which comprises identifying odorant ligands by the method mentioned in the preceding paragraph wherein the desired odorant receptor is that which is associated with the perception of food. Additionally, the invention provides a method of controlling appetite in a subject which comprises contacting the olfactory epithelium of the subject with these odorant ligands. Further the invention provides a nasal spray, to control appetite comprising the compounds identified by the above method in a suitable carrier.

The invention provides a method of trapping odors which comprises contacting a membrane which contains multiples of the desired odorant receptor, with a sample such that the desired odorant ligand is absorbed by the binding of the odorant ligand to the odorant receptor. The invention also provides an odor trap employing this method.

The invention also provides a method of controlling pest populations which comprises identifying odorant ligands by the method mentioned above which are alarm odorant ligands and spraying the desired area with the identified odorant ligands. Additionally, provided by the invention is a method of controlling a pest population which comprises identifying odorant ligands by the above mentioned method, which interfere with the interaction between the odorant ligands and the odorant receptors which are associated with fertility. In one embodiment the pest population is a population of insects or rodents, including mice and rats.

The invention also provides a method of promoting fertility which comprises identifying odorant ligands which interact with the odorant receptors associated with fertility by the above mentioned method. Further, the invention provides a

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method of inhibiting fertility which comprises employing the above mentioned method to identifying odorant ligands which inhibit the interaction between the odorant ligands and the odorant receptors associated with fertility.

5

This invention is illustrated in the Experimental Detail section which follow. These sections are set forth to aid in an understanding of the invention but are not intended to, and should not be construed to, limit in any way the invention as set forth in the claims which follow thereafter.

10

EXPERIMENTAL DETAILS

15

MATERIALS AND METHODS

Polymerase Chain Reaction

RNA was prepared from the olfactory epithelia of Sprague Dawley rats according to Chirgwin et al. (40) or using RNazol B (Cinna/Biotechx) and then treated with DNase I (0.1 unit/ μ g RNA) (Promega). In order to obtain cDNA, this RNA was incubated at 0.1 μ g/ μ l with 5 μ M random hexamers (Pharmacia) 1 mM each of dATP, dCTP, dGTP, TTP, and 2 units/ μ l RNase inhibitor (Promega) in 10 mM TrisCl (pH 8.3), 50 mM KCl, 2.5 mM $MgCl_2$, and 0.001% gelatin for 10 min. at 22°C, and then for a further 45 min. at 37°C following the addition of 20 u./ μ l of Moloney murine leukemia virus reverse transcriptase (BRL). After heating at 95°C for 3 min., cDNA prepared from 0.2 μ g of RNA was used in each of a series of polymerase chain reactions (PCR) containing 10 mM TrisCl (pH 8.3), 50 mM KCl, 1.5 mM $MgCl_2$, 0.001% gelatin, 200 μ M each of dATP, dCTP, dGTP, and TTP, 2.5 u. Taq polymerase (Perkin Elmer Cetus), and 2 μ M of each PCR

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primer. PCR reactions were performed according to the following schedule: 96°C for 45 sec., 55°C for 4 min. (or 45°C for 2 min.), 72°C for 3 min. with 6 sec. extension per cycle for 48 cycles. The primers used for PCR were a series of degenerate oligonucleotides made according to the amino acid sequences found in transmembrane domain 2 and 7 of a variety of different members of the 7 transmembrane domain protein superfamily (19). The regions used correspond to amino acids number 60-70 and 286-295 of clone I15 (Figure 4). Each of five different 5' primers were used in PCR reactions with each of six different 3' primers. The 5' primers had the sequences:

15 C AC A C CT
A1, AATTGGATICTIGTIAATCTIGCIGTIGCIGCIGA;

C C CA A C C
A2, AATTATTTTCTIGTIAATCTIGCITTIGCIGA;

20 CCA CC A C
A3, AATTITTATITATITCICTIGCITGIGCIGA;

A T C T ACT C
A4, CGITTICTIATGTGTAACCTITGCTTTGCIGA;

25 C CT TG
A5, ACIGTITATATIACICATCTIACIATIGCIGA.

The 3' primers were:

30 TTA T CAG C C A
B1, CTGICGGTTCATIAAIAACATAIATIGGGTT;

TG GA G G A A
35 B2, GATCGTTIAGACAACAATAIATIGGGTT;

A G G A
B3, TCIATGTTAAAIGTIGTATAIATIGGGTT;

40 T G G A A
B4, GCCTTIGTAAAIATIGCATAIAGGAAIGGGTT;

G AGA G G G A
45 B5, AAATCIGGGCTICGICAATAIATCAIIGGGTT;

CT CT G G G G A

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B6, GAIGAICCIACAAAAAATAIATAAAIGGGTT.

5 An aliquot of each PCR reaction was analyzed by agarose gel electrophoresis and bands of interest were amplified further by performing PCR reactions on pipet tip (approx. 1 μ l) plugs of the agarose gels containing those DNAs. Aliquots of these semi-purified PCR products were digested with the restriction enzymes Hae III or Hinf I and the digestion
10 products were compared with the undigested DNAs on agarose gels.

Isolation and Analysis of cDNA Clones

15 cDNA libraries were prepared according to standard procedures (41, 42) in the cloning vector, λ ZAP II (Stratagene) using poly A⁺ RNA prepared from Sprague Dawley rat epithelia (see above) or from an enriched population of olfactory neurons which had been obtained by a 'panning' procedure, using an antibody against the H blood group
20 antigen (Chembiomed) found on a large percentage of rat olfactory neurons. In initial library screens, 8.5×10^5 independent clones from the olfactory neuron library and 1.8×10^6 clones from the olfactory epithelium library were
25 screened (41) with a ³²P-labeled probe (prime-it, Stratagene) consisting of a pool of gel-isolated PCR products obtained using primers A4 and B6 (see above) in PCR reactions using as template, olfactory epithelium cDNA, rat liver DNA, or DNA prepared from the two cDNA libraries. In
30 later library screens, a mixture of PCR products obtained from 20 cDNA clones with the A4 and B6 primers was used as probe ('P1' probe). In initial screens, phage clones were analyzed by PCR using primers A4 and B6 and those which showed the appropriate size species were purified. In later
35 screens, all position clones were purified, but only those that could be amplified with the B6 primer and a primer

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specific for vector sequence were analyzed further. To obtain plasmids from the isolated phage clones, phagemid rescue was performed according to the instructions of the manufacturer of λ ZAP II (Stratagene). DNA sequence analysis was performed on plasmid DNAs using the Sequenase system (USB), initially with the A4 and B6 primers and later with oligonucleotide primers made according to sequences already obtained.

10 Northern and Southern Blot Analyses

For Northern blots, poly A⁺ RNAs from various tissues were prepared as described above or purchased from Clontech. One μ g of each RNA was size fractionated on formaldehyde agarose gels and blotted onto nylon membranes (41, 42). For Southern blots, genomic DNA prepared from Sprague Dawley rat liver was digested with the restriction enzymes Eco RI or Hind III, size fractionated on agarose gels and blotted onto nylon membranes (41, 42). The membranes were dried at 80°C, and then prehybridized in 0.5 M sodium phosphate buffer (pH 7.3) containing 1% bovine serum albumin and 4% sodium dodecyl sulfate. Hybridization was carried out in the same buffer at 65°-70°C for 14-20 hrs. with DNAs labeled with ³²P. For the first Northern blot shown, the 'P1' probe (see above under cDNA clone isolation) was used. For the second Northern blot shown, a mix of PCR fragments from seven divergent cDNA clones was used. For Southern blots, the region indicated in clone I15 by amino acids 118 through 251 was amplified from a series of divergent cDNA clones using PCR. The primers used for these reactions had the sequences:

P1, ATGGCITATGATCGITATGTIGC, and

35 P4, AAIAGIGAIACIATIGAIAGATGIGAICC

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These DNAs (or a DNA encompassing transmembrane domains 2 through 7 for clone F6) were labeled and tested for crosshybridization at 70°C. Those DNAs which did not show appreciable crosshybridization were hybridized individually, or as a pool to Southern blots at 70°C.

Rat Sequences used to obtain similar sequences expressed in Humans

There are genes similar to the rat genes discussed above present in humans, these genes may be readily isolated by screening human gene libraries with the cloned rat sequences or by performing PCR experiments on human genomic DNA with primers homologous to the rat sequences. First, PCR experiments were performed with genomic DNA from rat, human, mouse, and several other species. When primers homologous to transmembrane domains 2 and 6 (the A4/B6 primer set used to isolate the original rat sequences) were used, DNA of the appropriate size was amplified from rat, human and mouse DNAs. When these primary PCR reactions were subsequently diluted and subjected to PCR using primers to internal sequences (P1 and P4 primers), smaller DNA species were amplified whose size was that seen when the same primers were used in PCR reactions with the cloned rat cDNAs. Similarly, when the secondary PCR was performed with one outer primer together with one inner primer (ie. A4/P4 or P1/B6), amplified DNAs were obtained whose sizes were also consistent with the amplification of genes similar in sequence and organization to the cloned rat cDNAs. Second, a mix of segments from 20 of the rat cDNAs ('P1" probe) was used to screen libraries constructed from human genomic DNAs. Hybridization under high or low stringency conditions reveals the presence of a large number of cloned human DNA segments that are homologous to the rat sequences. Finally, RNA from a human olfactory tumor (neuroesthesioma,

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NCI-H-1011) cell line has been examined for sequences homologous to those cloned in the rat. cDNA prepared from this RNA was subjected to PCR with the A4/B6 primer set and a DNA species of the appropriate size was seen. This DNA
5 was subcloned and partially sequenced and clearly encodes a member of the olfactory protein family identified in the rat.

The inserted sequence in human clones H3/H5 was amplified by
10 PCR with the A4/B6 primers, gel purified, and then labeled with 32P. The labeled DNA was then hybridized to restriction enzyme human placenta. Multiple hybridizing species were observed with each DNA (See Figure 32). This observation is consistent with the presence of a family of
15 odorant receptor genes in the human genome.

The sequence of clone H5 is hereby shown in Figure 19. In addition, the translated protein sequence is shown in Figure
20 19.

In other to identify odorant receptors in other species, degenerated primer oligonucleotides homologous to conserved regions within the rat odorant receptor family may be used in PCR reactions with genomic DNA or with cDNA prepared from
25 olfactory tissue RNA from those species.

RESULTS

Cloning the Gene Family

30 A series of degenerate oligonucleotides were designated which could anneal to conserved regions of members of the superfamily of G-protein coupled seven transmembrane domain receptor genes. Five degenerate oligonucleotides (A1-5; see Experimental Procedures) matching sequences within
35 transmembrane domain 2, and six degenerate oligonucleotides

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(B1-6) matching transmembrane domain 7 were used in all combinations in PCR reactions to amplify homologous sequences in cDNA prepared from rat olfactory epithelium RNA. The amplification products of each PCR reaction were then analyzed by agarose gel electrophoresis. Multiple bands were observed with each of the primer combinations. The PCR products within the size range expected for this family of receptors (600 to 1300 bp) were subsequently picked and amplified further with the appropriate primer pair in order to isolate individual PCR bands. Sixty-four PCR bands isolated in this fashion revealed only one or a small number of bands upon agarose gel electrophoresis. Representatives of these isolated PCR products are shown in Figure 2A.

The isolated PCR products were digested with the endonuclease, Hae III or Hinf I, which recognize four base restriction sites and cut DNA at frequent intervals. In most instances, digestion of the PCR product with Hinf I generated a set of fragments whose molecular weights sum to the size of the original DNA (Figure 2B). These PCR bands are therefore likely to each contain a single DNA species. In some cases, however, restriction digestion yielded a series of fragments whose molecular weights sum to a value greater than that of the original PCR product. The most dramatic example is shown in Figure 2 where the 710 bp, PCR 13 DNA, is cleaved by Hinf I to yield a very large number of restriction fragments whose sizes sum to a value five- to ten-fold greater than that of the original PCR product. These observations indicated that PCR product 13 consists of a number of different species of DNA, each of which could be amplified with the same pair of primer oligonucleotides. In addition, when PCR experiments similar to those described were performed using cDNA library DNAs as templates, a 710 bp PCR product was obtained with the PCR13 primer pair

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(A4/B6) with DNA from olfactory cDNA libraries, but not a glioma cDNA library. Moreover, digestion of one of this 710 bp product also revealed the presence of multiple DNA species. In other cases (see PCR product 20, for example), digestion yielded a series of restriction fragments whose molecular weights also sum to a size greater than the starting material. Further analysis, however, revealed that the original PCR product consisted of multiple bands of similar but different sizes.

10

In order to determine whether the multiple DNA species present in PCR 13 encode members of a family of seven transmembrane domain proteins, PCR 13 DNA was cloned into the plasmid vector Bluescript and five individual clones were subjected to DNA sequence analysis. Each of the five clones exhibited a different DNA sequence, but each encoded a protein which displayed conserved features of the superfamily of seven transmembrane domain receptor proteins. In addition, the proteins encoded by all five clones shared distinctive sequence motifs not found in other superfamily members indicating they were all members of a new family of receptors.

20

To obtain full-length cDNA clones, cDNA libraries prepared from olfactory epithelium RNA or from RNA of an enriched population of olfactory sensory neurons were screened. The probe used in these initial screens was a mixture of PCR 13 DNA as well as DNA obtained by amplification of rat genomic DNA or DNA from two olfactory cDNA libraries with the same primers used to generate PCR 13 (A4 and B6 primers). Hybridizing plaques were subjected to PCR amplification with the A4/B6 primer set and only those giving a PCR product of the appropriate size (approximately 710 bp) were purified. The frequency of such positive clones in the enriched olfactory neuron cDNA library was approximately five times

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-25-

greater than the frequency in the olfactory epithelium cDNA library. The increased frequency of positive clones observed in the olfactory neuron library is comparable to the enrichment in olfactory neurons generally obtained in the purification procedure.

The original pair of primers used to amplify PCR 13 DNA were then used to amplify coding segments of 20 different cDNA clones. A mix of these PCR products were labeled and used as probe for further cDNA library screens. This mixed probe was also used in a Northern blot (Figure 3) to determine whether the expression of the gene family is restricted to the olfactory epithelium. The mixed probe detects two diffuse bands centered at 2 and 5 kb in RNA from olfactory epithelium; no hybridization can be detected in brain or spleen. (Later experiments which examined a larger number of tissue RNAs with a more restricted probe will be shown below.) Taken together, these data indicate the discovery of a novel multigene family encoding seven transmembrane domain proteins which are expressed in olfactory epithelium, and could be expressed predominantly or exclusively in olfactory neurons.

The Protein Sequences of Numerous, Olfactory-specific Members of the Seven Transmembrane Domain Superfamily

Numerous clones were obtained upon screening cDNA libraries constructed from olfactory epithelium and olfactory neuron RNA at high stringency. Partial DNA sequences were obtained from 36 clones; 18 of these cDNA clones are different, but all of them encode proteins which exhibit shared sequence motifs indicating that they are members of the family identified in PCR 13 DNA. A complete nucleotide sequence was determined for coding regions of ten of the most divergent clones (Figure 4). The deduced protein sequences

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of these cDNAs defines a new multigene family which shares sequence and structural properties with the superfamily of neurotransmitter and hormone receptors that traverse the membrane seven times. This novel family, however, exhibits
5 features different from any other member of the receptor superfamily thus far identified.

Each of the ten sequences contains seven hydrophobic stretches (19-26 amino acids) that represent potential
10 transmembrane domains. These domains constitute the regions of maximal sequence similarity to other members of the seven transmembrane domain superfamily (see legend to Figure 4). On the basis of structural homologies with rhodopsin and the β -adrenergic receptors, (19) it is likely that the amino
15 termini of the olfactory proteins are located on the extracellular side of the plasma membrane and the carboxyl termini are located in the cytoplasm. In this scheme, three extracellular loops alternate with three intracellular loops to link the seven transmembrane domains (see Figure 5).
20 Analysis of the sequences in figure 4 demonstrates that the olfactory proteins, like other members of the receptor superfamily, display no evidence of an N-terminal signal sequence. As in several other superfamily members, a potential N-linked glycosylation site is present in all ten
25 proteins within the short N-terminal extracellular segment. Other structural features conserved with previously identified members of the superfamily included cysteine residues at fixed positions within the first and second extracellular loops that are thought to form a disulfide
30 bond. Finally, many of the olfactory proteins reveal a conserved cysteine within the C-terminal domain which may serve as a palmitoylation site anchoring this domain to the membrane (21). These features, taken together with several short, conserved sequence motifs (see legend to Figure 4),
35 clearly define this new family as a member of the

-27-

superfamily of genes encoding the seven transmembrane domain receptors.

5 There are, however, important differences between the
olfactory protein family and the other seven transmembrane
domain proteins described previously and these differences
may be relevant to proposed function of these proteins in
odor recognition. Structure-function experiments involving
10 in vitro mutagenesis suggest that adrenergic ligands
interact with this class of receptor molecule by binding
within the plane of the membrane (22, 20). Not
surprisingly, small receptor families that bind the same
class of ligands, such as the adrenergic and muscarinic
acetylcholine receptor families exhibit maximum sequence
15 conservation (often over 80%) within the transmembrane
domains. In contrast, the family of receptors discussed in
this application shows striking divergence within the third,
fourth, and fifth transmembrane domains (Figure 4). The
variability in the three central transmembrane domains is
20 highlighted schematically in Figure 5. The divergence in
potential ligand binding domains is consistent with the idea
that the family of molecules cloned is capable of
associating with a large number of odorant of diverse
molecular structure.

25 Receptors which belong to the superfamily of seven
transmembrane domain proteins interact with G-proteins to
generate intracellular signals. In vitro mutagenesis
experiments indicate that one site of association between
30 receptor and G-protein resides within the third cytoplasmic
loop (22, 23). The sequence of this cytoplasmic loop in 18
different clones we have characterized is shown in Figure
6A. This loop which is often quite long and of variable
length in the receptor superfamily is relatively short (only
35 17 amino acids) and of fixed length in the 18 clones

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examined. Eleven of the 18 different clones exhibit the sequence motif K/R I V S S I (or a close relative) at the N-terminus of this loop. Two of the cDNA clones reveal a different H I T C/W A V motif at this site. If this short
5 loop is a site of contact with G-proteins, it is possible that the conserved motifs may reflect sites of interaction with different G-proteins that activate different intracellular signalling systems in response to odors. In addition, the receptors cloned reveal several serine or
10 threonine residues within the third cytoplasmic loop. By analogy with other G-protein coupled receptors, these residues may represent sites of phosphorylation for specific receptor kinases involved in desensitization. (24)

15 Subfamilies within the Multigene Family

Figure 6A displays the sequences of the fifth transmembrane domain and the adjacent cytoplasmic loop encoded by L8 of the cDNA clones we have analyzed. As a group, the 18
20 sequences exhibit considerable divergence within this region. The multigene family, however, can be divided into subfamilies such that the members of a given subfamily share significant sequence conservation. In subfamily B, clones F12 and F13, for example, differ from one another at only
25 four of 44 positions (91% identify), and clearly define a subfamily. Clones F5 and I11 (subfamily D) differ from F12 and F13 at 34-36 positions within this region and clearly define a separate subfamily. Thus, this olfactory-specific multigene family consists of highly divergent subfamilies.
30 If these genes encode odor receptors, it is possible that members of the divergent subfamilies bind odorant of widely differing structural classes. Members of the individual subfamilies could therefore recognize more subtle differences between molecules which belong to the same
35 structural class of molecules structures.

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The Size of the Multigene Family

Genomic Southern blotting experiments were performed and genomic libraries were screened to obtain an estimate of the sizes of the multigene family and the member subfamilies encoding the putative odor receptors. DNAs extending from the 3' end of transmembrane domain 3 to the middle of transmembrane domain 6 were synthesized by PCR from DNA of seven of the divergent cDNA clones (Figure 4). In initial experiments, these DNAs were labeled and hybridized to each other to define conditions under which minimal crosshybridization would be observed among the individual clones. At 70°C, the seven DNAs showed no crosshybridization, or crosshybridized only very slightly. The trace levels of crosshybridization observed are not likely to be apparent upon genomic Southern blot analysis where the amounts of DNA are far lower than in the test cross.

Probes derived from these seven DNAs were annealed under stringent conditions, either individually or as a group, to Southern blots of rat liver DNA digested with the restriction endonucleases Eco RI or Hind III (Figure 7). Examination of the Southern blots reveals that all but one of the cDNAs detects a relatively large, distinctive array of bands in genomic DNA. Clone I15 (probe 7), for example, detects about 17 bands with each restriction endonuclease, whereas clone F9 (probe 1) detects only about 5-7 bands with each enzyme. A single band is obtained with clone I7 (probe 5). PCR experiments using nested primers (TM2/TM7 primers followed by primers to internal sequences) and genomic DNA as template indicate that the coding regions of the members of this multigene family, like those of many members of the G-protein coupled superfamily, may not be interrupted by introns. This observation, together with the fact that most

-30-

of the probes only encompasses 400 nucleotides suggests that each band observed in these experiments is likely to represent a different gene. These data suggest that the individual probes chosen are representatives of subfamilies which range in size from a single member to as many as 17 members. A total of about 70 individual bands were detected in this analysis which could represent the presence of at least 70 different genes. Although the DNA probes used in these blots did not crosshybridize appreciably with each other, it is possible that a given gene might hybridize to more than one probe, resulting in an overestimate of gene number. However, it is probable that the total number of bands only reflects a minimal estimate of gene number since it is unlikely that we have isolated representative cDNAs from all of the potential subfamilies and the hybridizations were performed under conditions of very high stringency.

A more accurate estimate of the size of the olfactory-specific gene family was obtained by screening rat genomic libraries. The mix of the seven divergent probes used in Southern blots, or the mix of 20 different probes used in our initial Northern blots (see Figure 3), were used as hybridization probes under high (65°C) or lowered (55°C) stringency conditions in these experiments. Nested PCR (see above) was used to verify that the clones giving a positive signal under low stringency annealing conditions were indeed members of this gene family. It is estimated from these studies that there are between 100 and 200 positive clones per haploid genome. The estimate of the size of the family obtain from screens of genomic libraries again represents a lower limit. Given the size of the multigene family, one might anticipate that many of these genes are linked such that a given genomic clone may contain multiple genes. Thus the data from Southern blotting and screens of genomic libraries indicate that the multigene family identified

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consists of one to several hundred member genes which can be divided into multiple subfamilies.

5 It should be noted that the cDNA probes isolated may not be representative of the full complement of subfamilies within the larger family of olfactory proteins. The isolation of cDNAs, for example, relies heavily on PCR with primers from transmembrane domains 2 and 7 and biases our clones for homology within these regions. Thus, estimates of gene
10 number as well as subsequent estimates of RNA abundance should be considered as minimal.

Expression of the Members of this Multigene Family

15 Additional Northern blot analyses were performed to demonstrate that expression of the members of this gene family is restricted to the olfactory epithelium. (Figure 8) Northern blot analysis with a mixed probe consisting of the seven divergent cDNAs used above reveals two diffuse bands
20 about 5 and 2 kb in length in olfactory epithelium RNA. This pattern is the same as that seen previously with the mix of 20 DNAs. No annealing is observed to RNA from the brain or retina or other, nonneural tissues, including lung, liver, spleen, and kidney.

25 An estimate of the level of expression of this family can be obtained from screens of cDNA libraries. The frequency of positive clones in cDNA libraries made from olfactory epithelium RNA suggests that the abundance of the RNAs in
30 the epithelium is about one in 20,000. The frequency of positive clones is approximately five-fold higher in a cDNA library prepared from RNA from purified olfactory neurons (in which 75% of the cells are olfactory neurons). The increased frequency of positive clones obtained in the
35 olfactory neuron cDNA library is comparable to the

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enrichment we obtain upon purification of olfactory neurons. These observations suggest that this multigene family is expressed largely, if not solely, in olfactory neurons and may not be expressed in other cell types within the epithelium. If each olfactory neuron contains 10^5 mRNA molecules, from the frequency of positive clones we predict that each neuron contains only 25-30 transcripts derived from this gene family. Since the family of olfactory proteins consists of a minimum of a hundred genes, a given olfactory neuron could maximally express only a proportion of the many different family members. These values thus suggest that olfactory neurons will exhibit significant diversity at the level of expression of these olfactory proteins.

15

Identification of pheromone receptors in vomeronasal organ

The vomeronasal organ (vomeronasal gland) is an accessory olfactory structure that is located near the nasal cavity. Like the olfactory epithelium of the nasal cavity, the olfactory epithelium of the vomeronasal organ contains olfactory sensory neurons. The vomeronasal organ is believed to play an important role in the sensing of pheromones in numerous species. Pheromones are believed to have profound effects on both physiological and behavioral aspects of reproduction. the identification of pheromone receptors would permit the identification of the pheromones themselves. It would also enable one to identify agonists or antagonists that would either mimic the pheromones or block the pheromone receptors from transducing pheromone signals. Such information would be important to the development of species specific pesticides and, conversely, to animal husbandry. The identification of pheromone receptors in human could ultimately lead to the development of contraceptives or to treatments for infertility in humans. It is likely that the identification of pheromone receptors

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in low mammals such as rodents would lead to the identification of similar receptors in human.

5 In order to identify potential pheromone receptors, we isolate RNA from the vomeronasal organs of female rats and prepared cDNA from this RNA. The cDNA was subjected to PCR with several different pairs of degenerate oligonucleotide primers that match sequences present in the rat odorant receptor family. The PCR products were subcloned and the
10 nucleotide sequences of the subcloned DNAs were determined. Each of the subcloned DNAs encodes a protein that belongs to the odorant receptor family. The sequences of the following vomeronasal subclones are shown: J1, J2, J4, J7, J8, J11, J14, J15, J16, J17, J19, J20. In a few cases (J2, J4), the
15 same sequence was amplified with two different primer pairs and the sequence shown is a composite of the two sequences. It is possible that one or more of these molecules, or closely related molecules, serve as pheromone receptors in the rat.

20

DISCUSSION

The mammalian olfactory system can recognize and discriminate a large number of odorous molecules.
25 Perception in this system, as in other sensory systems, initially involves the recognition of external stimuli by primary sensory neurons. This sensory information is then transmitted to the brain where it is decoded to permit the discrimination of different odors. Elucidation of the logic
30 underlying olfactory perception is likely to require the identification of the specific odorant receptors, the analysis of the extent of receptor diversity and receptor specificity, as well as an understanding of the pattern of receptor expression in the olfactory epithelium.

35

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The odorant receptors are thought to transduce intracellular signals by interacting with G-proteins which activate second messenger systems (12, 13, 14, 15). These proteins are clearly members of the family of G-protein coupled receptors which traverse the membrane seven times (19). The odorant receptors should be expressed specifically in the tissue in which odorant are recognized. The family of olfactory proteins cloned is expressed in the olfactory epithelium. Hybridizing RNA is not detected in brain or retina, or in a host of nonneural tissues. Moreover, expression of this gene family the epithelium may be restricted to olfactory neurons. The family of odorant receptors must be capable of interacting with extremely diverse molecular structures. The genes cloned are members of any extremely large multigene family which exhibit variability in regions thought to be important in ligand binding. The possibility that each member of this large family of seven transmembrane proteins is capable of interacting with only one or a small number of odorant provides a plausible mechanism to accommodate the diversity of odor perception. The properties of the gene family identified suggests that this family is likely to encode a large number of distinct odorant receptors.

25 Size of the Multigene Family

The size of the receptor repertoire is likely to reflect the range of detectable odors and the degree of structural specificity exhibited by the individual receptors. It has been estimated that humans can identify over 10,000 structurally-distinct odorous ligands. However, this does not necessarily imply that humans possess an equally large repertoire of odorant receptors. For example, binding studies in lower vertebrates suggest that structurally-related odorant may activate the same receptor molecules.

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In fish which smell amino acids, the binding of alanine to isolated cilia can be competed by other small polar residues (threonine and serine), but not by the basic amino acids, lysine or arginine (11). These data suggest that individual
5 receptors are capable of associating with several structurally-related ligands, albeit with different affinities. Stereochemical models of olfactory recognition in mammals (25) (based largely on psychophysical, rather than biophysical data) have suggested existence of several
10 primary odor groups including camphoraceous, musky, peppermint, ethereal, pungent, and putrid. In such a model, each group would contain odorant with common molecular configurations which bind to common receptors and share similar odor qualities.

15 Screens of genomic libraries with mixed probes consisting of divergent family members detect approximately 100 to 200 positive clones per genome. The present estimate of at least 100 genes provides only a lower limit since it is
20 likely that the probes used do not detect all of the possible subfamilies. Moreover, it is probable that many of these genes are linked such that a given genomic clone may contain multiple genes. It is therefore expected that the actual size of the gene family may be considerably higher
25 and this family of putative odorant receptors could constitute one of the largest gene families in the genome.

The characterization of a large multigene family encoding putative odorant receptors suggests that the olfactory
30 system utilizes a far greater number of receptors than the visual system. Color vision, for example, allows the discrimination of several hundred hues, but is accomplished by only three different photoreceptors (1, 2, 3 and 4). The photoreceptors each have different, but overlapping
35 absorption spectra which cover the entire spectrum of

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visible wavelengths. Discrimination of color results from comparative processing of the information from these three classes of photoreceptors in the brain. Whereas three photoreceptors can absorb light across the entire visible spectrum, our data suggest that a small number of odorant receptors cannot recognize and discriminate the full spectrum of distinct molecular structures perceived by the mammalian olfactory system. Rather, olfactory perception probably employs an extremely large number of receptors each capable of recognizing a small number of odorous ligands.

Diversity within the Gene Family and the Specificity of Odor Recognition

The olfactory proteins identified in this application are clearly members of the superfamily of receptors which traverse the membrane seven time. Analysis of the proteins encoded by the 18 distinct cDNAs we have cloned reveals structural features which may render this family particularly well suited for the detection of a diverse array of structurally distinct odorant. Experiments with other members of this class of receptors suggest that the ligand binds to its receptor within the plane of the membrane such that the ligand contacts many, if not all of the transmembrane helices. The family of olfactory proteins can be divided into several different subfamilies which exhibit significant sequence divergence within the transmembrane domains. Nonconservative changes are commonly observed within blocks of residues in transmembrane regions 3, 4, and 5 (Figures 4, 5, 6); these blocks could reflect the sites of direct contact with odorous ligands. Some members, for example, have acidic residues in transmembrane domain 3, which in other families are thought to be essential for binding aminergic ligands (20) while other members maintain hydrophobic residues at these positions.

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This divergence within transmembrane domains may reflect the fact that the members of the family of odorant receptors must associate with odorant of widely different molecular structures.

5

These observations suggest a model in which each of the individual subfamilies encode receptors which bind distinct structural classes of odorant. Within a given subfamily, however, the sequence differences are far less dramatic and are often restricted to a small number of residues. Thus, the members of a subfamily may recognize more subtle variations among odor molecules of a given structural class. At a practical level, individual subfamilies may recognize grossly different structures such that one subfamily may associate, for example, with the aromatic compound, benzene and its derivatives, whereas a second subfamily may recognize odorous, short chain, aliphatic molecules. Subtle variations in the structure of the receptors within, for example, the hypothetical benzene subfamily could facilitate the recognition and discrimination of various substituted derivatives such as toluene, xylene or phenol. It should be noted that such a model, unlike previous stereochemical models, does not necessarily predict that molecules with similar structures will have similar odors. The activation of distinct receptors with similar structures could elicit different odors, since perceived odor will depend upon higher order processing of primary sensory information.

30

Evolution of the Gene Family and the Generation of Diversity

Preliminary evidence from PCR analyses suggests that members of this family of olfactory proteins are conserved in lower vertebrates as well as invertebrates. This gene family presumably expanded over evolutionary time providing mammals with the ability to recognize an increasing diversity of

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odorant. Examination of the sequences of the family members cloned from mammals provides some insight into the evolution of this multigene family. Although the chromosomal loci encoding these genes has yet to be characterized, it is likely that at least some member genes will be tandemly arranged in a large cluster as is observed with other large multigene families. A tandem array of this sort provides a template for recombination events including unequal crossing over and gene conversion, that can lead to expansion and further diversification of the sort apparent among the family members we have cloned (26).

The multigene family encoding the olfactory proteins is large: all of the member genes clearly have a common ancestral origin, but have undergone considerable divergence such that individual genes encode proteins that share from 40-80% amino acid identity. Subfamilies are apparent with groups of genes sharing greater homology among themselves than with members of other subfamilies. Examination of the sequences of even the most divergent subfamilies, however, reveals a pattern in which several blocks of conserved residues are interspersed with variable regions. This segmental homology is conceptually similar to the organization of framework and hypervariable domains within the families of immunoglobulin and T cell receptor variable region sequences (27, 28). This analogy goes beyond structural organization and may extend to the function of these two gene families: each family consists of a large number of genes which have diversified over evolutionary time to accommodate the binding of a highly diverse array of ligands. The evolutionary mechanisms responsible for the diversification and maintenance of these large gene families may also be similar. It has been suggested that gene conversion has played a major role in the evolution of immunoglobulin and T cell receptor variable domains (29, 30).

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- and 31). Analysis of the sequence of the putative olfactory receptors reveals at least one instance where a motif from a variable region of one subfamily is found imbedded in the otherwise divergent sequence of a second subfamily, suggesting that conversion has occurred. Such a mixing of motifs from one subfamily to another over evolutionary time would provide additional combinatorial possibilities leading to the generation of diversity.
- It should be noted, however, that the combinatorial joining of gene segments by DNA rearrangement during development, which is characteristic of immunoglobulin loci (27), is not a feature of the putative odor receptor gene family. No evidence for DNA rearrangement to generate the diversity of genes cloned has been observed. The entire coding region has been sequenced along with parts of the 5' and 3' untranslated regions of 10 different cDNA clones. The sequences of the coding regions are all different; no evidence has been obtained for constant regions that would suggest DNA rearrangement of the sort seen in the immune system. The observations indicate that the diversity olfactory proteins are coded by a large number of distinct gene sequences.
- Although it is unlikely from the data that DNA rearrangement is responsible for the generation of diversity among the putative odorant receptors, it remains possible that DNA rearrangements may be involved in the regulation of expression of this gene family. If each olfactory neuron expresses only one or a small number of genes, then a transcriptional control mechanism must be operative to choose which of the more than one hundred genes within the family will be expressed in a given neuron. Gene conversion from one of multiple silent loci into a single active locus, as observed for the trypanosome-variable surface

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glycoproteins (32), provides one attractive model. The gene conversion event could be stochastic, such that a given neuron could randomly express any one of several hundred receptor genes, or regulated (perhaps by positional information), such that a given neuron could only express one or a small number of predetermined receptor types. Alternatively, it is possible that positional information in the olfactory epithelium controls the expression of the family of olfactory receptors by more classical mechanisms that do not involve DNA rearrangement. What ever mechanisms will regulate the expression of receptor genes within this large, multigene family, these mechanisms must accommodate the requirement that olfactory neurons are regenerated every 30-60 days (8) and therefore the expression of the entire repertoire of receptors must be accomplished many times during the life of an organism.

Receptor Diversity and the Central Processing of Olfactory Information

The results suggest the existence of a large family of distinct odorant receptors. Individual members of this receptor family are likely to be expressed by only a small set of the total number of olfactory neurons. The primary sensory neurons within the olfactory epithelium will therefore exhibit significant diversity at the level of receptor expression. The question then emerges as to whether neurons expressing the same receptors are localized in the olfactory epithelium. Does the olfactory system employ a topographic map to discriminate among the numerous odorant? The spatial organization of distinct classes of olfactory sensory neurons, as defined by receptor expression, can now be determined by using the procedures of in situ hybridization and immunohistochemistry with probes specific for the individual receptor subtypes. This

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information should help to distinguish between different models that have been proposed to explain the coding of diverse odorant stimuli (33).

5 In one model, sensory neurons that express a given receptor and respond to a given odorant may be localized within defined positions within the olfactory epithelium. This topographic arrangement would also be reflected in the projection of olfactory sensory axons into discrete regions
10 (glomeruli) within the olfactory bulb. In this scheme, the central coding to permit the discrimination of discrete odorant would depend, in part, on the spatial segregation of different receptor populations. Attempts to discern the topographic localization of specific receptors at the level
15 of the olfactory epithelium has led to conflicting results. In some studies, electrophysiological recordings have revealed differences in olfactory responses to distinct odorant in different regions of the olfactory epithelium (34, 35). However, these experiments have been difficult to
20 interpret since the differences in response across the epithelium are often small and are not observed in all studies (36).

A second model argues that sensory neurons expressing
25 distinct odorant receptors are randomly distributed in the epithelium but that neurons responsive to a given odorant project to restricted regions within the olfactory bulb. In this instance, the discrimination of odors would be a consequence of the position of second order neurons in the olfactory bulb, but would be independent of the site of
30 origin of the afferent signals within the epithelium. Mapping of the topographic projections of olfactory neurons has been performed by extracellular recordings from different regions of the bulb (37, 38) and by 2-deoxyglucose
35 autoradiography to map regional activity after exposure to

-42-

- different odorant (39). These studies suggest that spatially-localized groups of bulbar neurons preferentially respond to different odorant. The existence of specific odorant receptors, randomly distributed through the olfactory epithelium, which converge on a common target within the olfactory bulb, would raise additional questions about the recognition mechanisms used to guide these distinct axonal subsets to their central targets.
- Other sensory systems also spatially segregate afferent input from primary sensory neurons. The spatial segregation of information employed, for example, by the visual and somatosensory systems, is used to define the location of the stimulus within the external environment as well as to indicate the quality of the stimulus. In contrast, olfactory processing does not extract spatial features of the odorant stimulus. Relieved of the necessity to encode information about the spatial localization of the sensory stimulus, it is possible that the olfactory system of mammals uses the spatial segregation of sensory input solely to encode the identity of the stimulus itself. The molecular identification of the genes likely to encode a large family of olfactory receptors should provide initial insights into the underlying logic of olfactory processing in the mammalian nervous system.

-43-

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SEQUENCE LISTING

(1) GENERAL INFORMATION:

- (i) APPLICANT: Columbia University in the City of N.Y.,
The Trustees of
- (ii) TITLE OF INVENTION: ODORANT RECEPTORS AND USES THEREOF
- (iii) NUMBER OF SEQUENCES: 36
- (iv) CORRESPONDENCE ADDRESS:
 - (A) ADDRESSEE: COOPER & DUNHAM
 - (B) STREET: 30 Rockefeller Plaza
 - (C) CITY: New York
 - (D) STATE: New York
 - (E) COUNTRY: U.S.A.
 - (F) ZIP: 10112
- (v) COMPUTER READABLE FORM:
 - (A) MEDIUM TYPE: Floppy disk
 - (B) COMPUTER: IBM PC compatible
 - (C) OPERATING SYSTEM: PC-DOS/MS-DOS
 - (D) SOFTWARE: PatentIn Release #1.0, Version #1.25
- (vii) PRIOR APPLICATION DATA:
 - (A) APPLICATION NUMBER: US 681,880
 - (B) FILING DATE: 05-APR-1991
- (viii) ATTORNEY/AGENT INFORMATION:
 - (A) NAME: White, John P.
 - (B) REGISTRATION NUMBER: 28,678
 - (C) REFERENCE/DOCKET NUMBER: 38586
- (ix) TELECOMMUNICATION INFORMATION:
 - (A) TELEPHONE: (212) 977-9550
 - (B) TELEFAX: (212) 664-0525
 - (C) TELEX: (212) 422523 COOP UI

(2) INFORMATION FOR SEQ ID NO:1:

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 954 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: single
 - (D) TOPOLOGY: linear
- (ii) MOLECULE TYPE: cDNA
- (iii) HYPOTHETICAL: YES
- (iv) ANTI-SENSE: NO
- (vi) ORIGINAL SOURCE:
 - (A) ORGANISM: rat olfactory epithelium
 - (B) STRAIN: Sprague-Dawley rat
 - (F) TISSUE TYPE: olfactory epithelium
- (vii) IMMEDIATE SOURCE:

SUBSTITUTE SHEET

-50-

(B) CLONE: F12

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- (A) LENGTH: 1002 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA

(iii) HYPOTHETICAL: YES

(iv) ANTI-SENSE: NO

(vi) ORIGINAL SOURCE:

- (A) ORGANISM: rat olfactory epithelium
- (B) STRAIN: Sprague-Dawley rat
- (F) TISSUE TYPE: olfactory epithelium

(vii) IMMEDIATE SOURCE:

- (B) CLONE: F3

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:2:

SUBSTITUTE SHEET

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(2) INFORMATION FOR SEQ ID NO:3:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 942 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA

(iii) HYPOTHETICAL: YES

(iv) ANTI-SENSE: NO

(vi) ORIGINAL SOURCE:

- (A) ORGANISM: rat olfactory epithelium
- (B) STRAIN: Sprague-Dawley rat
- (F) TISSUE TYPE: olfactory epithelium

(vii) IMMEDIATE SOURCE:

- (B) CLONE: F5

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:3:

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CTGTATTTTC TCGCTGTGTT TGGTAACATG GACAATTTC TCGTGGCTGT GATGTCCTAT      360
GACCGATTTC TGGCCATATG CCACCCCTTA CACTACACAA CAAAGATGAC CCGTCAGCTC      420
TGTGTCCTGC TTGTTGTGGG GTCATGGGTT GTAGCCAACA TGAATTGTCT GTTGACATA      480
CTGCTCATGG CTGACTCTC CTTCTGTGCA GACAACATGA TCCCCACTT CTTCTGTGAT      540
GGAACTCCCC TCCTGAACT CTCCTGCTCA GACACACATC TCAATGAGCT GATGATTCTT      600
ACAGAGGGAG CTGTGGTCAT GGTACCCCCA TTTGTCTGCA TCCTCATCTC CTACATCCAC      660
ATCACCTGTG CTGTCCTCAG AGTCTCATCC CCCAGGGGAG GATGGAAATC CTTCTCCACC      720
TGTGGCTCCC ACCTGGCTGT GGTCTGCCTC TTCTATGGCA CCGTCATCGC TGTGTATTTTC      780
AACCCTCATC CCTCTCACTT AGCTGGGAGG GACATGGCAG CTGCAGTGAT GTATGCAGTG      840
GTGACCCCAA TGCTGAACCC TTTCATCTAT AGCCTGAGGA ACAGCCACAT GAAAGCAGCT      900
TTAAGGAAAG TGCTGCCAT GAGATTTCCA TCTAAGCAGT AA                          942

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(2) INFORMATION FOR SEQ ID NO:4:

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 936 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: single
 - (D) TOPOLOGY: linear
- (ii) MOLECULE TYPE: cDNA
- (iii) HYPOTHETICAL: YES
- (iv) ANTI-SENSE: NO
- (v) ORIGINAL SOURCE:
 - (A) ORGANISM: rat olfactory epithelium
 - (B) STRAIN: Sprague-Dawley rat
 - (F) TISSUE TYPE: olfactory epithelium
- (vii) IMMEDIATE SOURCE:
 - (B) CLONE: F6

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:4:

```

ATGGCTTCCA GTACTGGCCA GAACCTGTCC ACACCAGGAC CATTATCTT GCTGGGCTTC      60
CCAGGGCCAA GGAGCATGCG CATTGGGCTC TTCCTGCTTT TCCTGGTCAT GTATCTGCTT      120
ACGGTAGTTG GAAACCTAGC CATCATCTCC CTGGTAGGTG CCCACAGATG CCTACAGACA      180
CCCATGTACT TCTTCCTCTG CAACCTCTCC TTCCTGGAGA TCTGGTTCAC CACAGCCTGC      240
GTACCCAAGA CCCTGGCCAC ATTTGCGCCT CGGGGTGGAG TCATTTCCTT GGCTGGCTGT      300

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GCCACACAGA TGTACTTTGT CTTTCTTTG GGCTGTACOG AGTACTTCCT GCTGGCTGTG      360
ATGGCTTATG ACOGCTACCT GGCCATCTGC CTGCCACTGC GCTATGGTGG CATCATGACT      420
CCTGGGCTGG CGATGCGGTT GGCCCTGGGA TCCTGGCTGT GTGGGTTTTT TGCAATCACA      480
GTTCTGCTA CCCTCATTGC CCGCCTCTCT TTCTGTGGCT CACGTGTCAT CAACCACTTC      540
TTCTGTGACA TTTCGCCCTG GATAGTGCTT TCCTGCACCG ACACGCAGGT GGTGGAAGTG      600
GTGTCCTTTG GCATTGCCTT CTGTGTTATT CTGGGCTCGT GTGGTATCAC ACTAGTCTCC      660
TATGCTTACA TCATCACTAC CATCATCAAG ATTCCCTCTG CCGGGGGCCG GCACCGCGCC      720
TTCTCAACCT GCTCATCCCA TCTCACTGTG GTGCTGATTT GGTATGGCTC CACCATCTTC      780
TTGCATGTGA GGACCTCGGT AGAGAGCTCC TTGGACCTCA CCAAAGCTAT CACAGTGCTC      840
AACACCATTG TCACACCTGT GCTGAACCCT TTCATATATA CTCTGAGGAA CAAGGATGTC      900
AAGGAAGCTC TGCGCAGGAC GGTGAAGGGG AAGTGA                                936

```

(2) INFORMATION FOR SEQ ID NO:5:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 939 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA

(iii) HYPOTHETICAL: YES

(iv) ANTI-SENSE: NO

(vi) ORIGINAL SOURCE:

- (A) ORGANISM: rat olfactory epithelium
- (B) STRAIN: Sprague-Dawley rat
- (F) TISSUE TYPE: olfactory epithelium

(vii) IMMEDIATE SOURCE:

- (B) CLONE: I14

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:5:

```

ATGACTGGAA ATAACCAAAC TTTGATCTTG GAGTTCCTCC TCCTGGGTCT GCCCATCCCA      60
TCAGAGTATC ATCTCCTGTT CTATGCCCTG TTCCTGGCCA TGTACCTCAC CATCATCCTG      120
GGAAACCTGC TAATCATTGT CTTGTTTGA CTGGACTCTC ATCTCCACAT GCCCATGTAC      180
TTGTTTCTCA GCAACTTGTC CTTCTCTGAC CTCTGCTTTT CCTCTGTAC AATGCCCAA      240
TTGCTTCAGA ACATGCAGAG CCAAGTACCA TCTATATCCT ATACAGGCTG CCTGACACAG      300
CTGTACTTCT TTATGGTTTT TGGAGATATG GAGAGCTTCC TTCTTGTTGGT CATGGCCTAT      360
GACCGCTATG TGGCCATTG CTTTCCTTTG CGTTACACCA CCATCATGAG CACCAAGTTC      420
TGTGCTTCAC TAGTGCTACT TCTGTGGATG CTGACGATGA CCCATGCCCT GCTGCATACC      480

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CTACTCATTG CTAGATTGTC TTTTGTGAG AAGAATGTGA TTCTTCACTT TTTCTGTGAC 540
ATTTCTGCTC TTCTGAAGTT GTCTGCTCA GACATTTATG TTAATGAGCT GATGATATAT 600
ATCTTGGGTG GACTCATCAT TATTATCCCA TTCCTATTAA TTGTTATGTC CTATGTTAGA 660
ATTTTCTTCT CCATTTTGAA GTTCCATCT ATTCAAGACA TCTACAAGGT ATTCTCAACC 720
TGTGGTTCCC ATCTGTCTGT GGTGACCTTG TTTTATGGGA CAATTTTGG TATCTACTTA 780
TGTCCATCAG GTAATAATTC TACTGTGAAG GAGATTGCCA TGGCTATGAT GTACACAGTG 840
GTGACTCCCA TGCTGAATCC CTTTCTCTAC AGCCTGAGGA ACAGAGACAT GAAAAGGGCC 900
CTAATAAGAG TTATCTGCAC TAAGAAAATC TCTCTGTAA 939

(2) INFORMATION FOR SEQ ID NO:6:

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 945 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: single
 - (D) TOPOLOGY: linear
- (ii) MOLECULE TYPE: cDNA
- (iii) HYPOTHETICAL: YES
- (iv) ANTI-SENSE: NO
- (vi) ORIGINAL SOURCE:
 - (A) ORGANISM: rat olfactory epithelium
 - (B) STRAIN: Sprague-Dawley rat
 - (F) TISSUE TYPE: olfactory epithelium
- (vii) IMMEDIATE SOURCE:
 - (B) CLONE: 115

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:6:

ATGACAGAAG AGAACCAAC TGTGATCTCC CAGTTCCTTC TCCTTTTCCT GCCCATCCCC 60
TCAGAGCACC AGCACGTGT CTACGCCCTG TTCCTGTCCA TGTACCTCAC CACTGTCTCTG 120
GGGAACCTCA TCATCATCAT CCTCATTAC CTGGACTCCC ATCTCCACAC ACCCATGTAC 180
TTGTTTCTCA GCAACTTGTC CTTCTCTGAT CTCTGCTTTT CCTCTGTTAC GATGCCCAAG 240
TTGTTGCAGA ACATGCAGAG CCAAGTTCCA TCCATCCCCT TTGCAGGCTG CCTGACACAA 300
TTATACTTTT ACCTGTATTT TGCAGACCTT GAGAGCTTCC TGCTTGTCGC CATGGCCTAT 360
GACCGCTATG TGGCCATCTG CTTCCCCCTT CATTACATGA GCATCATGAG CCCCAGCTC 420
TGTGTGAGTC TGGTGGTGCT GTCCTGGGTG CTGACCACCT TCCATGCCAT GCTGCACACC 480
CTGCTCATGG CCAGATTGTC ATTCTGTGCG GACAATATGA TCCCCCACTT TTTCTGTGAT 540
ATATCTCCTT TATTGAAACT GTCCTGCTCT GACACGCATG TTAATGAGTT GGTGATATTT 600

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GTGATGGGAG GGCTTGTTAT TGTGATTCCA TTTGTGCTCA TCATTGTATC TTATGCACGA	660
GTTGTGCGCT CCATTCTTAA AGTCCCTTCT GTCCGAGGCA TCCACAAGAT CTTCTCCACC	720
TGCGGCTCCC ATCTGTCTGT GGTGTCACCTG TTCTATGGGA CAATCATTGG TCTCTACTTA	780
TGTCCGTCAG CTAATAACTC TACTGTGAAG GAGACTGTCA TGGCCATGAT GTACACACTG	840
GTGACCCCCA TGCTGAACCC CTTTCATCTAC AGCCTGAGGA ACAGAGACAT GAAAGAGGCA	900
CTGATAAGAG TCCTTTGTAA AAAGAAAATT ACCTTCTGTC TATGA	945

(2) INFORMATION FOR SEQ ID NO:7:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 933 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA

(iii) HYPOTHETICAL: YES

(iv) ANTI-SENSE: NO

(vi) ORIGINAL SOURCE:

- (A) ORGANISM: rat olfactory epithelium
- (B) STRAIN: Sprague-Dawley rat
- (F) TISSUE TYPE: olfactory epithelium

(vii) IMMEDIATE SOURCE:

- (B) CLONE: I3

(x1) SEQUENCE DESCRIPTION: SEQ ID NO:7:

ATGAACAATC AAACCTTCAT CACCCAATTC CTTCTCCTGG GACTGCCCAT CCCTGAAGAA	60
CATCAGCACC TGTCTATGC CTGTTCTCTG GTCATGTACC TCACCACCAT CTTGGGAAAC	120
TTGCTAATCA TTGTAATTGT TCAACTGGAC TCCCAGCTCC ACACACCTAT GTATTTGTTT	180
CTCAGCAATT TGTCTTTCTC TGATCTATGT TTTTCCTCTG TCACAATGCC CAAGCTGCTG	240
CAGAACATGA GGAGCCAGGA CACATCCATT CCCTATGGAG GCTGCCTGGC ACAAACATAC	300
TTCTTTATGG TTTTGGGAGA TATGGAGAGT TTCCTTCTTG TGGCCATGGC CTATGACCGC	360
TATGTGGCCA TCTGCTTCCC TCTGCATTAC ACCAGCATCA TGAGCCCCAA GCTCTGTACT	420
TGTCTAGTGC TGTTATTGTG GATGCTGAGC ACATCCCATG CCATGATGCA CACACTGCTT	480
GCAGCAAGAT TGTCTTTTGG TGAGAACAAT GTGGTCCTCA ACTTCTTCTG TGACCTATTT	540
GTTCTCCTAA AGCTGGCCTG CTCAGACACT TATATTAATG AGTTGATGAT ATTTATCATG	600
AGTACACTCC TCATTATTAT TCCATTCTTC CTCATTGTGA TGTCTATGC AAGGATCATA	660
TCCTCTATTC TTAAGGTTCC ATCTACCCAA GGCATCTGCA AGGTCTTCTC TACCTGTGGT	720

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TCCCATCTGT CTGTAGTATC ACTGTTCTAT GGGACAATTA TTGGTCTCTA CTTATGTCCA	780
GCAGGTAATA ATTCCACTGT AAAAGAGATG GTCATGGCCA TGATGTACAC TGTGGTGACC	840
CCCATGCTGA ATCCCTTCAT CTACAGCCTA AGGAATAGAG ATATGAAGAG GGCCCTAATA	900
AGAGTTATCT GTAGTATGAA AATCACTCTG TAA	933

(2) INFORMATION FOR SEQ ID NO:8:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 984 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA

(iii) HYPOTHETICAL: YES

(iv) ANTI-SENSE: NO

(vi) ORIGINAL SOURCE:

- (A) ORGANISM: rat olfactory epithelium
- (B) STRAIN: Sprague-Dawley rat
- (F) TISSUE TYPE: olfactory epithelium

(vii) IMMEDIATE SOURCE:

- (B) CLONE: I7

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:8:

ATGGAGCGAA GGAACCACAG TGGGAGAGTG AGTGAATTTG TGTGCTGGG TTTCCCAGCT	60
CCTGCCCCAC TGGGAGTACT ACTATTTTTC CTTTCTCTTC TGGACTATGT GTTGGTGTTG	120
ACTGAAAACA TGCTCATCAT TATAGCAATT AGGAACCACC CAACCCTCCA CAAACCCATG	180
TATTTTCTCT TGGCTAATAT GTCATTTCTG GAGATTTGGT ATGTCACGTG TACGATTCTT	240
AAGATGCTCG CTGGCTTCAT TGGTTCCAAG GAGAACCATG GACAGCTGAT CTCCTTTGAG	300
GCATGCATGA CACAACCTCA CTTTTTCCTG GGCTTGGGTT GCACAGAGTG TGTCTTCTT	360
GCTGTGATGG CCTATGACCG CTATGTGGCT ATCTGTCATC CACTCCACTA CCCCGTCATT	420
GTCAGTAGCC GGCTATGTGT GCAGATGGCA GCTGGATCCT GGGCTGGAGG TTTTGGTATC	480
TCCATGGTTA AAGTTTTCTT TATTCTCGC CTGTCTTACT GTGGCCCCAA CACCATCAAC	540
CACTTTTTCT GTGATGTGTC TCCATTGCTC AACCTGTCAT GCACTGACAT GTCCACAGCA	600
GAGCTTACAG ACTTTGTCCT GGCCATTTTT ATTCTGCTGG GACCGCTCTC TGTCAGTGGG	660
GCATCCTACA TGGCCATCAC AGGTGCTGTG ATCGCATCC CCTCAGCTGC TGGCCGCCAT	720
AAAGCCTTTT CAACCTGTGC CTCCACCTC ACTGTTGTGA TCATCTTCTA TGCAGCCAGT	780
ATTTTCATCT ATGCCAGGCC TAAGGCACTC TCAGCTTTTG ACACCAACAA GCTGGTCTCT	840
GTA CTCTACG CTGTCAATTGT ACCGTTGTTT AATCCCATCA TCTACTGCTT GCGCAACCAA	900

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GATGTCAAAA GAGCGCTACG TCGCAOGCTG CACCTGGCCC AGGACCAGGA GGCCAATACC 960
 AACAAAGGCA GCAAAATTGG TTAG 984

(2) INFORMATION FOR SEQ ID NO:9:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 939 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA

(iii) HYPOTHETICAL: YES

(iv) ANTI-SENSE: NO

(v) ORIGINAL SOURCE:

- (A) ORGANISM: rat olfactory epithelium
- (B) STRAIN: Sprague-Dawley rat
- (F) TISSUE TYPE: olfactory epithelium

(vi) IMMEDIATE SOURCE:

- (B) CLONE: 18

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:9:

ATGAACAACA AACTGTGTCAT CACCCATTTC CTCCTCCTGG GATTGCCCAT CCCCCAGAG 60
 CACCAGCAAC TGTTCCTTGC CCGTTCCTG ATCATGTACC TCACCACCTT TCTGGGAAAC 120
 CTGCTAATTG TTGTCCTTGT TCAACTGGAC TCTCATCTCC ACACACCCAT GTACTTGTTT 180
 CTCAGCAACT TGTCTTCTC TGATCTCTGC TTTTCCTCTG TTACAATGCT GAAATTGCTG 240
 CAAAATATAC AGAGCCAAGT ACCATCTATA TCCTATGCAG GATGCCTGAC ACAGATATTC 300
 TTCTTTTGT TGTITGGCTA CCGTGGGAAT TTCCTTCTG TAGCCATGGC CTATGACCGC 360
 TATGTGGCCA TCTGCTTCCC TCTGCATTAT ACCAACATCA TGAGCCATAA GCTCTGTACT 420
 TGTCTCCTGC TGGTATTTTG GATAATGACA TCATCTCATG CCATGATGCA CACCCTGCTT 480
 GCAGCAAGAT TGTCTTTTGG TGAGAACAAT GTACTCCTCA ACTTTTCTG TGACCTGTTT 540
 GTTCTCCTAA AGTTGGCCTG CTCAGACACT TATGTTAATG AGTTGATGAT ACATATCATG 600
 GCGGTGATCA TCATTGTTAT TCCATTGGTG CTCATTGTTA TATCCTATGC CAAGATCATC 660
 TCCTCCATTTC TTAAGGTTCC ATCTACTCAA AGCATTACACA AGGTCTTCTC CACTTGCGGT 720
 TCTCATCTCT CTGTGGTGTC TCTGTTCTAC GGGACAATTA TTGGTCTCTA TTTATGTCCA 780
 TCAGGTGATA ATTTTAGTCT AAAGGGGTCT GCCATGGCTA TGATGTACAC AGTGGTAACT 840
 CCAATGCTGA ACCCGTTCAT CTACAGCCTA AGAAACAGAG ACATGAAGCA GGCCCTAATA 900
 AGAGTTACCT GTAGCAAGAA AATCTCTCTG CCATGCTAG 939

(2) INFORMATION FOR SEQ ID NO:10:

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- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 945 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: single
 - (D) TOPOLOGY: linear
- (ii) MOLECULE TYPE: cDNA
- (iii) HYPOTHETICAL: YES
- (iv) ANTI-SENSE: NO
- (vi) ORIGINAL SOURCE:
 - (A) ORGANISM: rat olfactory epithelium
 - (B) STRAIN: Sprague-Dawley rat
 - (F) TISSUE TYPE: olfactory epithelium
- (vii) IMMEDIATE SOURCE:
 - (B) CLONE: 19

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:10:

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ATGACTAGAA GAAACCAAC TGCCATCTCT CAGTTCTTCC TTCTGGGCCT GCCATTCCCC      60
CCAGAGTACC AACACCTGTT CTATGCCCTG TTCTGGCCA TGTACCTCAC CACTCTCCTG      120
GGGAACCTCA TCATCATCAT CCTCATTCTA CTGGACTCCC ATCTCCACAC ACCCATGTAC      180
TTGTTTCTCA GCAATTTATC CTTTGGCGAC CTCTGTTTTT CCTCTGTAC AATGCCCAAG      240
TTGTTGCAGA ACATGCAGAG CCAAGTTCCA TCCATCCCCT ATGCAGGGTG CCTGGCACAG      300
ATATACTTCT TTCTGTTTTT TGGAGACCTT GGAAACTTCC TGCTTGTGGC CATGGCCTAT      360
GACCGCTATG TGGCATCTG CTTCGCCCTT CATTACATGA GCATCATGAG CCCCAGCTC      420
TGTGTGAGTC TGGTGGTGCT GTCTGGGTG CTGACTACCT TCCATGCCAT GCTGCACACC      480
CTGCTCATGG CCAGATTGTC ATTCTGTGAG GACAGTGTA TCCCTCACTA TTTCTGTGAT      540
ATGTCTACTC TGCTGAAAGT GGCTTGTCT GACACCCATG ATAATGAATT AGCAATATTT      600
ATCTTAGGGG GCCCTATAGT TGTACTACCT TTCCTTCTCA TCATTGTTTC TTATGCAAGA      660
ATTGTTTCCT CCATCTTCAA GGTCCCTTCT TCTCAAAGCA TCCATAAAGC CTTCTCCACC      720
TGTGGCTCCC ACCTGTCTGT GGTGTCACGT TTCTATGGGA CAGTCATTGG TCTCTACTTA      780
TGTCCCTCAG CTAATAACTC CACTGTGAAG GAGACTGTCA TGTCTTTGAT GTACACAATG      840
GTGACACCCA TGCTGAACCC CTTCATCTAC AGCCTAAGAA ACAGAGACAT AAAAGATGCA      900
TTAGAAAAAA TAATGTGCAA AAAGCAAATT CCCTCCTTTC TATGA                      945

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(2) INFORMATION FOR SEQ ID NO:11:

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 645 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: single
 - (D) TOPOLOGY: linear

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(ii) MOLECULE TYPE: cDNA
(iii) HYPOTHETICAL: YES
(iv) ANTI-SENSE: NO
(vi) ORIGINAL SOURCE:
      (A) ORGANISM: homosapien
(vii) IMMEDIATE SOURCE:
      (B) CLONE: H5
(ix) FEATURE:
      (A) NAME/KEY: CDS
      (B) LOCATION: 1..645
```

(x1) SEQUENCE DESCRIPTION: SEQ ID NO:11:

ATC Ile 1	TGT Cys	TTT Phe	GTG Val	TCT Ser 5	ACC Thr	ACT Thr	GTC Val	CCA Pro	AAG Lys 10	CAG Gln	CTG Leu	GTG Val	AAC Asn	ATC Ile 15	CAG Gln	48
ACA Thr	CAG Gln	AGC Ser	AGA Arg 20	GTC Val	ATC Ile	ACC Thr	TAT Tyr	GCA Ala 25	GAC Asp	TGC Cys	ATC Ile	ACC Thr	CAG Gln 30	ATG Met	TGC Cys	96
TTT Phe	TTT Phe	ATA Ile 35	CTC Leu	TTT Phe	GTA Val	GTG Val	TTG Leu 40	GAC Asp	AGC Ser	TTA Leu	CTC Leu	CTG Leu 45	ACT Thr	GTG Val	ATG Met	144
GCC Ala	TAT Tyr 50	GAC Asp	CGG Arg	TTT Phe	GTG Val	GCC Ala 55	ATC Ile	TGT Cys	CAC His	CCC Pro	CTG Leu 60	CAC His	TAC Tyr	ACA Thr	GTC Val	192
ATT Ile 65	ATG Met	AGC Ser	TCC Ser	TGG Trp	CTC Leu 70	TGT Cys	GGA Gly	CTG Leu	CTG Leu 75	GTT Val	CTG Leu	GTG Val	TCC Ser	TGG Trp	ATC Ile 80	240
GTG Val	AGC Ser	ATC Ile	CTA Leu	TAT Tyr 85	TCT Ser	CTG Leu	TTA Leu	CAA Gln	AGC Ser 90	ATA Ile	ATG Met	GCA Ala	TTG Leu	CAG Gln 95	CTG Leu	288
TCC Ser	TTC Phe	TGT Cys	ACA Thr 100	GAA Glu	CTG Leu	AAA Lys	ATC Ile	CCT Pro 105	CAA Gln	TTT Phe	TTC Phe	TGT Cys	GAA Glu 110	CTT Leu	AAT Asn	336
CAG Gln	GTC Val	ATC Ile 115	CAC His	CTT Leu	GCC Ala	TGT Cys	TCC Ser 120	GAC Asp	ACT Thr	TTT Phe	ATT Ile	AAT Asn 125	GAC Asp	ATG Met	ATG Met	384
ATG Met	AAT Asn 130	TTT Phe	ACA Thr	AGT Ser	GTG Val	CTG Leu 135	CTG Leu	GGT Gly	GGG Gly	GGA Gly	TGC Cys 140	CTC Leu	GCT Ala	GGA Gly	ATA Ile	432
TTT Phe 145	TAC Tyr	TNN Xaa	TAC Tyr	TTT Phe	AAG Lys 150	ATA Ile	CTT Leu	TGT Cys	TGC Cys	ATA Ile 155	TGT Cys	TCG Ser	ATC Ile	TCA Ser	TCA Ser 160	480
GCT Ala	CAG Gln	GGG Gly	ATG Met	AAT Asn 165	AAA Lys	GCA Ala	CTT Leu	TCC Ser	ACC Thr 170	TGT Cys	GCA Ala	TCT Ser	CAC His	CTC Leu 175	TCA Ser	528

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GTT GTC TCC TTA TTT TAT TGT ACA GGC GTA OGT GTG TAC CTT AGT TCT	576
Val Val Ser Leu Phe Tyr Cys Thr Gly Val Gly Val Tyr Leu Ser Ser	
180 185 190	
GCT GCA ACC CAT AAC TCA CTC TCA AAT GCT GCA GCC TCG GTG ATG TAC	624
Ala Ala Thr His Asn Ser Leu Ser Asn Ala Ala Ala Ser Val Met Tyr	
195 200 205	
ACT GTG GTC ACC TCC ATG CTG	645
Thr Val Val Thr Ser Met Leu	
210 215	

(2) INFORMATION FOR SEQ ID NO:12:

- (i) SEQUENCE CHARACTERISTICS:
 (A) LENGTH: 215 amino acids
 (B) TYPE: amino acid
 (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:12:

Ile Cys Phe Val Ser Thr Thr Val Pro Lys Gln Leu Val Asn Ile Gln	
1 5 10 15	
Thr Gln Ser Arg Val Ile Thr Tyr Ala Asp Cys Ile Thr Gln Met Cys	
20 25 30	
Phe Phe Ile Leu Phe Val Val Leu Asp Ser Leu Leu Leu Thr Val Met	
35 40 45	
Ala Tyr Asp Arg Phe Val Ala Ile Cys His Pro Leu His Tyr Thr Val	
50 55 60	
Ile Met Ser Ser Trp Leu Cys Gly Leu Leu Val Leu Val Ser Trp Ile	
65 70 75 80	
Val Ser Ile Leu Tyr Ser Leu Leu Gln Ser Ile Met Ala Leu Gln Leu	
85 90 95	
Ser Phe Cys Thr Glu Leu Lys Ile Pro Gln Phe Phe Cys Glu Leu Asn	
100 105 110	
Gln Val Ile His Leu Ala Cys Ser Asp Thr Phe Ile Asn Asp Met Met	
115 120 125	
Met Asn Phe Thr Ser Val Leu Leu Gly Gly Gly Cys Leu Ala Gly Ile	
130 135 140	
Phe Tyr Xaa Tyr Phe Lys Ile Leu Cys Cys Ile Cys Ser Ile Ser Ser	
145 150 155 160	
Ala Gln Gly Met Asn Lys Ala Leu Ser Thr Cys Ala Ser His Leu Ser	
165 170 175	
Val Val Ser Leu Phe Tyr Cys Thr Gly Val Gly Val Tyr Leu Ser Ser	
180 185 190	
Ala Ala Thr His Asn Ser Leu Ser Asn Ala Ala Ala Ser Val Met Tyr	
195 200 205	

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Thr Val Val Thr Ser Met Leu
210 215

(2) INFORMATION FOR SEQ ID NO:13:

(1) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 640 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA

(iii) HYPOTHETICAL: YES

(iv) ANTI-SENSE: NO

(vi) ORIGINAL SOURCE:

- (A) ORGANISM: rat olfactory epithelium
- (B) STRAIN: Sprague-Dawley rat
- (F) TISSUE TYPE: olfactory epithelium

(vii) IMMEDIATE SOURCE:

- (B) CLONE: J1

(ix) FEATURE:

- (A) NAME/KEY: CDS
- (B) LOCATION: 2..640

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:13:

C ATC TGC TTT ACT TCT GCT AGC ATC CCA AAG ATG CTA GTG AAT ATA	46
Ile Cys Phe Thr Ser Ala Ser Ile Pro Lys Met Leu Val Asn Ile	
1 5 10 15	
CAG ACG AAG AAC AAG GTG ATC ACC TAT GAA GGC TGC ATC TCC CAA GTA	94
Gln Thr Lys Asn Lys Val Ile Thr Tyr Glu Gly Cys Ile Ser Gln Val	
20 25 30	
TAC TTT TCA TAC TCT TTG GAG TTT TGG ACA ACT TTC TTC TCG ACT GTG	142
Tyr Phe Ser Tyr Ser Leu Glu Phe Trp Thr Thr Phe Phe Ser Thr Val	
35 40 45	
ATG GCC TAT GAC CGA TAT GTG GCC ATC TGT CAC CCA TCT NAC TAC ACA	190
Met Ala Tyr Asp Arg Tyr Val Ala Ile Cys His Pro Ser Xaa Tyr Thr	
50 55 60	
GGT CAT CAT GAA CCN NNN NNN NNN NNN NNN NNN NNN NNN NNN NNN	238
Gly His His Glu Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa	
65 70 75	
NNN NNN NNN NNN NNN NNN NNN NNN NNN NNN NNN NNN NNN NNN	286
Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa	
80 85 90 95	
NNN NNN NNN NNN NNN NNN NNN NNN NNN NNN NNN NNN NNN NNN	334
Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa	
100 105 110	
NNN NNN NNN NNN NNN NNN NNN NNN NNN NNN NNN NNN NNN NNN	382
Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa	

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115	120	125	
NNN NNN NNN NNN NNN NNN NNN NNN NNN NNN NNN NNN NNN NNN NNN NTT			430
Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa			
130	135	140	
TAT TCT TAC TCT AAG ATA GTT TCC TCC ATA CGA GAA ATC TCA TCA TCA			478
Tyr Ser Tyr Ser Lys Ile Val Ser Ser Ile Arg Glu Ile Ser Ser Ser			
145	150	155	
CAG GGA AAG TAC AAG NNA TTC TCC ACC TGT GCA TCC CAC CTC TCA GTT			526
Gln Gly Lys Tyr Lys Xaa Phe Ser Thr Cys Ala Ser His Leu Ser Val			
160	165	170	175
GTT TCA TTA TTC TAT TCT ACA CTT TTG GGT GTG TAC CTT AGT TCT TCT			574
Val Ser Leu Phe Tyr Ser Thr Leu Leu Gly Val Tyr Leu Ser Ser Ser			
180	185	190	
TTT ACC CAA AAC TCA CAC TCA ACT GCA CGG GCA TCT GTT ATG TAC AGT			622
Phe Thr Gln Asn Ser His Ser Thr Ala Arg Ala Ser Val Met Tyr Ser			
195	200	205	
GTG GTC ACC CCC ATG TTG			640
Val Val Thr Pro Met Leu			
210			

(2) INFORMATION FOR SEQ ID NO:14:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 213 amino acids

(B) TYPE: amino acid

(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:14:

Ile	Cys	Phe	Thr	Ser	Ala	Ser	Ile	Pro	Lys	Met	Leu	Val	Asn	Ile	Gln
1				5					10					15	
Thr	Lys	Asn	Lys	Val	Ile	Thr	Tyr	Glu	Gly	Cys	Ile	Ser	Gln	Val	Tyr
		20						25					30		
Phe	Ser	Tyr	Ser	Leu	Glu	Phe	Trp	Thr	Thr	Phe	Phe	Ser	Thr	Val	Met
		35					40					45			
Ala	Tyr	Asp	Arg	Tyr	Val	Ala	Ile	Cys	His	Pro	Ser	Xaa	Tyr	Thr	Gly
	50					55					60				
His	His	Glu	Xaa	Xaa	Xaa	Xaa	Xaa	Xaa	Xaa	Xaa	Xaa	Xaa	Xaa	Xaa	Xaa
65				70				75						80	
Xaa	Xaa	Xaa	Xaa	Xaa	Xaa	Xaa	Xaa	Xaa	Xaa	Xaa	Xaa	Xaa	Xaa	Xaa	Xaa
			85					90					95		
Xaa	Xaa	Xaa	Xaa	Xaa	Xaa	Xaa	Xaa	Xaa	Xaa	Xaa	Xaa	Xaa	Xaa	Xaa	Xaa
		100					105						110		
Xaa	Xaa	Xaa	Xaa	Xaa	Xaa	Xaa	Xaa	Xaa	Xaa	Xaa	Xaa	Xaa	Xaa	Xaa	Xaa
	115						120						125		

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Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Tyr
 130 135 140
 Ser Tyr Ser Lys Ile Val Ser Ser Ile Arg Glu Ile Ser Ser Ser Gln
 145 150 155 160
 Gly Lys Tyr Lys Xaa Phe Ser Thr Cys Ala Ser His Leu Ser Val Val
 165 170 175
 Ser Leu Phe Tyr Ser Thr Leu Leu Gly Val Tyr Leu Ser Ser Ser Phe
 180 185 190
 Thr Gln Asn Ser His Ser Thr Ala Arg Ala Ser Val Met Tyr Ser Val
 195 200 205
 Val Thr Pro Met Leu
 210

(2) INFORMATION FOR SEQ ID NO:15:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 636 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

(iii) HYPOTHETICAL: YES

(iv) ANTI-SENSE: NO

(vi) ORIGINAL SOURCE:

- (A) ORGANISM: rat olfactory epithelium
- (B) STRAIN: srpague-Dawley rat
- (F) TISSUE TYPE: olfactory epithelium

(vii) IMMEDIATE SOURCE:

- (B) CLONE: J2

(ix) FEATURE:

- (A) NAME/KEY: CDS
- (B) LOCATION: 1..636

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:15:

ACC TCC ACC ACC ATC CCA AAG ATG CTG GTA AAT ATA CAC ACC CAG AGC	48
Thr Ser Thr Thr Ile Pro Lys Met Leu Val Asn Ile His Thr Gln Ser	
1 5 10 15	
AAT ACT ATC ACC TAT GAA GAC TGT ATT TCC CAG ATG TTT GTA CTC TTG	96
Asn Thr Ile Thr Tyr Glu Asp Cys Ile Ser Gln Met Phe Val Leu Leu	
20 25 30	
GTT TTT GGA GAA CTG GAC AAC TTT CTC CTG GCT GTG ATG GCC TAT GAT	144
Val Phe Gly Glu Leu Asp Asn Phe Leu Leu Ala Val Met Ala Tyr Asp	
35 40 45	
CGA TAT GTG GCT ATC TGT CAC CCA CTG TAT TAC ACA GTC ATT GTG AAC	192
Arg Tyr Val Ala Ile Cys His Pro Leu Tyr Tyr Val Ile Val Asn	
50 55 60	

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CAC CGA CTC TGT ATC CTG CTG CTT CTG CTG TCC TGG GTT GTC AGC ATT His Arg Leu Cys Ile Leu Leu Leu Leu Leu Ser Trp Val Val Ser Ile 65 70 75 80	240
TTA CAT GCC TTC TTA CAG AGC TTA ATT GTA CTA CAG TTG ACC TTC TGT Leu His Ala Phe Leu Gln Ser Leu Ile Val Leu Gln Leu Thr Phe Cys 85 90 95	288
GGA GAT GTG AAA ATC CCT CAC TTC TTC TGT GAG CTC AAT CAG CTG TCC Gly Asp Val Lys Ile Pro His Phe Phe Cys Glu Leu Asn Gln Leu Ser 100 105 110	336
CAA CTC ACA TGT TCA GAC AAC TTT CCA AGT CAC CTC ACA ATG CAT CTT Gln Leu Thr Cys Ser Asp Asn Phe Pro Ser His Leu Thr Met His Leu 115 120 125	384
GTA CCT GTT ATA TTT GCA GCT ATT TCC CTC AGT GGT ATC CTT TAC TCT Val Pro Val Ile Phe Ala Ala Ile Ser Leu Ser Gly Ile Leu Tyr Ser 130 135 140	432
TAT TTC AAG ATA GTG TCT TCC ATA CGT TCT ATG TCC TCA GTT CAA GGG Tyr Phe Lys Ile Val Ser Ser Ile Arg Ser Met Ser Ser Val Gln Gly 145 150 155 160	480
AAG TAC AAG GCA TTT TCT ACA TGT GCC TCT CAC CTT TCC ATT GTC TCC Lys Tyr Lys Ala Phe Ser Thr Cys Ala Ser His Leu Ser Ile Val Ser 165 170 175	528
TTA TTT TAT AGT ACA GGC CTC GGG GTG TAC GTC AGT TCT GCT GTG ATC Leu Phe Tyr Ser Thr Gly Leu Gly Val Tyr Val Ser Ser Ala Val Ile 180 185 190	576
CGA AGC TCA CAC TCC TCT GCA AGT GCT TCG GTC ATG TAT ACT GTG GTC Arg Ser Ser His Ser Ser Ala Ser Ala Ser Val Met Tyr Thr Val Val 195 200 205	624
ACC CCC ATG TTG Thr Pro Met Leu 210	636

(2) INFORMATION FOR SEQ ID NO:16:

- (i) SEQUENCE CHARACTERISTICS:
 (A) LENGTH: 212 amino acids
 (B) TYPE: amino acid
 (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:16:

Thr Ser Thr Thr Ile Pro Lys Met Leu Val Asn Ile His Thr Gln Ser
1 5 10 15

Asn Thr Ile Thr Tyr Glu Asp Cys Ile Ser Gln Met Phe Val Leu Leu
20 25 30

Val Phe Gly Glu Leu Asp Asn Phe Leu Leu Ala Val Met Ala Tyr Asp
35 40 45

Arg Tyr Val Ala Ile Cys His Pro Leu Tyr Tyr Thr Val Ile Val Asn

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50	55	60
His Arg Leu Cys Ile Leu Leu Leu Leu Ser Trp Val Val Ser Ile		
65	70	75 80
Leu His Ala Phe Leu Gln Ser Leu Ile Val Leu Gln Leu Thr Phe Cys		
	85	90 95
Gly Asp Val Lys Ile Pro His Phe Phe Cys Glu Leu Asn Gln Leu Ser		
	100	105 110
Gln Leu Thr Cys Ser Asp Asn Phe Pro Ser His Leu Thr Met His Leu		
	115	120 125
Val Pro Val Ile Phe Ala Ala Ile Ser Leu Ser Gly Ile Leu Tyr Ser		
	130	135 140
Tyr Phe Lys Ile Val Ser Ser Ile Arg Ser Met Ser Ser Val Gln Gly		
	145	150 155 160
Lys Tyr Lys Ala Phe Ser Thr Cys Ala Ser His Leu Ser Ile Val Ser		
	165	170 175
Leu Phe Tyr Ser Thr Gly Leu Gly Val Tyr Val Ser Ser Ala Val Ile		
	180	185 190
Arg Ser Ser His Ser Ser Ala Ser Ala Ser Val Met Tyr Thr Val Val		
	195	200 205
Thr Pro Met Leu		
210		

(2) INFORMATION FOR SEQ ID NO:17:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 646 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA

(iii) HYPOTHETICAL: YES

(iv) ANTI-SENSE: NO

(vi) ORIGINAL SOURCE:

- (A) ORGANISM: rat olfactory epithelium
- (B) STRAIN: erpague-Dawley rat
- (F) TISSUE TYPE: olfactory epithelium

(vii) IMMEDIATE SOURCE:

- (B) CLONE: J4

(ix) FEATURE:

- (A) NAME/KEY: CDS
- (B) LOCATION: 2..646

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:17:

C ATA GGC TAT TCA TCT TCT GTC ACA CCC AAT ATG CTT GTC AAC TTC

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Ile	Gly	Tyr	Ser	Ser	Ser	Val	Thr	Pro	Asn	Met	Leu	Val	Asn	Phe		
1				5					10					15		
CTT	ATA	AAG	CAA	AAT	ACC	ATC	TCA	TAC	CTT	GGA	TGT	TCT	ATA	CAG	TTT	94
Leu	Ile	Lys	Gln	Asn	Thr	Ile	Ser	Tyr	Leu	Gly	Cys	Ser	Ile	Gln	Phe	
				20					25					30		
GGC	TCA	GCT	GCT	TTG	TTT	GGA	GGT	CTT	GAA	TGC	TTC	CTT	CTG	GCT	GCC	142
Gly	Ser	Ala	Ala	Leu	Phe	Gly	Gly	Leu	Glu	Cys	Phe	Leu	Leu	Ala	Ala	
			35					40					45			
ATG	GCG	TAT	GAT	CGT	TTT	GTA	GCA	ATC	TGC	AAC	CCA	CTG	CTT	TAT	TCA	190
Met	Ala	Tyr	Asp	Arg	Phe	Val	Ala	Ile	Cys	Asn	Pro	Leu	Leu	Tyr	Ser	
		50					55					60				
ACG	AAA	ATG	TCC	ACA	CAA	GTC	TGT	GTC	CAG	TTG	GTT	GTG	GGA	TCT	TAT	238
Thr	Lys	Met	Ser	Thr	Gln	Val	Cys	Val	Gln	Leu	Val	Val	Gly	Ser	Tyr	
	65					70					75					
ATA	GCG	GGA	TTT	CTT	AAT	GCC	TCC	TCT	TTT	ACC	CTT	TCC	TTT	TTT	TCC	286
Ile	Gly	Gly	Phe	Leu	Asn	Ala	Ser	Ser	Phe	Thr	Leu	Ser	Phe	Phe	Ser	
	80				85				90						95	
TTG	TCC	TTC	TGT	GGA	CCA	AAT	AGA	ATC	AAT	CAC	TTT	TAC	TGT	GAT	TTT	334
Leu	Ser	Phe	Cys	Gly	Pro	Asn	Arg	Ile	Asn	His	Phe	Tyr	Cys	Asp	Phe	
				100					105					110		
GCT	CCG	TTA	GTA	GAA	CTT	TCT	TGC	TCT	GAT	GTC	AGT	GTT	CCT	GAT	GCT	382
Ala	Pro	Leu	Val	Glu	Leu	Ser	Cys	Ser	Asp	Val	Ser	Val	Pro	Asp	Ala	
			115					120					125			
GTT	ACC	TCA	TTT	TCT	GCT	GCC	TCA	GTT	ACT	ATG	CTC	ACA	GTG	TTT	ATC	430
Val	Thr	Ser	Phe	Ser	Ala	Ala	Ser	Val	Thr	Met	Leu	Thr	Val	Phe	Ile	
		130					135					140				
ATA	GCC	ATC	TCC	TAT	ACC	TAT	ATC	CTC	ATC	ACC	ATC	CTG	AAG	ATG	CGT	478
Ile	Ala	Ile	Ser	Tyr	Thr	Tyr	Ile	Leu	Ile	Thr	Ile	Leu	Lys	Met	Arg	
	145					150					155					
TCC	ACT	GAG	GGT	CGA	CAG	AAA	GCA	TTC	TCT	ACC	TGC	ACT	TCC	CAC	CTC	526
Ser	Thr	Glu	Gly	Arg	Gln	Lys	Ala	Phe	Ser	Thr	Cys	Thr	Ser	His	Leu	
	160				165					170					175	
ACT	GCA	GTC	ACT	CTG	TGC	TAT	GGA	ACC	ATC	ACA	TTC	ATC	TAT	GTG	ATG	574
Thr	Ala	Val	Thr	Leu	Cys	Tyr	Gly	Thr	Ile	Thr	Phe	Ile	Tyr	Val	Met	
				180					185					190		
CCC	AAG	TCC	AGC	TAC	TCC	ACA	GAC	CAG	AAC	AAG	GTG	GTG	TCT	GTG	TTT	622
Pro	Lys	Ser	Ser	Tyr	Ser	Thr	Asp	Gln	Asn	Lys	Val	Val	Ser	Val	Phe	
			195					200					205			
TAT	ATG	GTG	GTG	ATC	CCC	ATG	TTG									646
Tyr	Met	Val	Val	Ile	Pro	Met	Leu									
		210					215									

(2) INFORMATION FOR SEQ ID NO:18:

(1) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 215 amino acids
- (B) TYPE: amino acid
- (D) TOPOLOGY: linear

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(ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:18:

```

Ile Gly Tyr Ser Ser Ser Val Thr Pro Asn Met Leu Val Asn Phe Leu
 1           5           10           15
Ile Lys Gln Asn Thr Ile Ser Tyr Leu Gly Cys Ser Ile Gln Phe Gly
 20           25           30
Ser Ala Ala Leu Phe Gly Gly Leu Glu Cys Phe Leu Leu Ala Ala Met
 35           40           45
Ala Tyr Asp Arg Phe Val Ala Ile Cys Asn Pro Leu Leu Tyr Ser Thr
 50           55           60
Lys Met Ser Thr Gln Val Cys Val Gln Leu Val Val Gly Ser Tyr Ile
 65           70           75           80
Gly Gly Phe Leu Asn Ala Ser Ser Phe Thr Leu Ser Phe Phe Ser Leu
 85           90           95
Ser Phe Cys Gly Pro Asn Arg Ile Asn His Phe Tyr Cys Asp Phe Ala
100          105          110
Pro Leu Val Glu Leu Ser Cys Ser Asp Val Ser Val Pro Asp Ala Val
115          120          125
Thr Ser Phe Ser Ala Ala Ser Val Thr Met Leu Thr Val Phe Ile Ile
130          135          140
Ala Ile Ser Tyr Thr Tyr Ile Leu Ile Thr Ile Leu Lys Met Arg Ser
145          150          155          160
Thr Glu Gly Arg Gln Lys Ala Phe Ser Thr Thr Cys Thr Ser His Leu Thr
165          170          175
Ala Val Thr Leu Cys Tyr Gly Thr Ile Thr Phe Ile Tyr Val Met Pro
180          185          190
Lys Ser Ser Tyr Ser Thr Asp Gln Asn Lys Val Val Ser Val Phe Tyr
195          200          205
Met Val Val Ile Pro Met Leu
210          215

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(2) INFORMATION FOR SEQ ID NO:19:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 481 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA

(iii) HYPOTHETICAL: YES

(iv) ANTI-SENSE: NO

(vi) ORIGINAL SOURCE:

- (A) ORGANISM: rat olfactory epithelium

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(B) STRAIN: Sprague-Dawley rat
(F) TISSUE TYPE: o'factory epithelium

(vii) IMMEDIATE SOURCE:
(B) CLONE: J7

(ix) FEATURE:
(A) NAME/KEY: CDS
(B) LOCATION: 2..481

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:19:

C ATC TGC AAG CCC CTG CAC TAC ACC ACC ATC ATG AAT AAC CGA GTG Ile Cys Lys Pro Leu His Tyr Thr Thr Ile Met Asn Asn Arg Val 1 5 10 15	46
TGC ACA GTT CTA GTC CTC TCC TGT TGG TTT GCT GGC CTG TTG ATC ATC Cys Thr Val Leu Val Leu Ser Cys Trp Phe Ala Gly Leu Leu Ile Ile 20 25 30	94
CTC CCA CCT CTT GGT CAT GGC CTC CAG CTG GAG TTC TGT GAC TCC AAT Leu Pro Pro Leu Gly His Gly Leu Gln Leu Glu Phe Cys Asp Ser Asn 35 40 45	142
GTG ATT GAT CAT TTT GGC TGT GAT GCC TCT CCA ATT CTG CAG ATA ACC Val Ile Asp His Phe Gly Cys Asp Ala Ser Pro Ile Leu Gln Ile Thr 50 55 60	190
TGC TCA GAC ACG GTA TTT ATA GAG AAA ATT GTC TTG GCT TTT GCC ATA Cys Ser Asp Thr Val Phe Ile Glu Lys Ile Val Leu Ala Phe Ala Ile 65 70 75	238
CTG ACA CTC ATC ATT ACT CTG GTA TGT GTT GTT CTC TCC TAC ACA TAC Leu Thr Leu Ile Ile Thr Leu Val Cys Val Val Leu Ser Tyr Thr Tyr 80 85 90 95	286
ATC ATC AAG ACC ATT TTA AAG TTT CCT TCT GCT CAA CAA AGA AAA AAG Ile Ile Lys Thr Ile Leu Lys Phe Pro Ser Ala Gln Gln Arg Lys Lys 100 105 110	334
GCC TTT TCT ACA TGT TCT TCC CAC ATG ATT GTG GTT TCC ATC ACC TAT Ala Phe Ser Thr Cys Ser Ser His Met Ile Val Val Ser Ile Thr Tyr 115 120 125	382
GGG AGC TGT ATT TTC ATC TAC ATC AAA CCT TCA GCG AAG GAA GGG GTA Gly Ser Cys Ile Phe Ile Tyr Ile Lys Pro Ser Ala Lys Glu Gly Val 130 135 140	430
GCC ATC AAT AAG GTT GTA TCT GTG CTC ACA ACA TCA GTC GCC CCT TTG Ala Ile Asn Lys Val Val Ser Val Leu Thr Thr Ser Val Ala Pro Leu 145 150 155	478
CTC Leu 160	481

(2) INFORMATION FOR SEQ ID NO:20:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 160 amino acids

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(B) TYPE: amino acid
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:20:

```

Ile Cys Lys Pro Leu His Tyr Thr Thr Ile Met Asn Asn Arg Val Cys
 1           5           10           15
Thr Val Leu Val Leu Ser Cys Trp Phe Ala Gly Leu Leu Ile Ile Leu
      20           25           30
Pro Pro Leu Gly His Gly Leu Gln Leu Glu Phe Cys Asp Ser Asn Val
      35           40           45
Ile Asp His Phe Gly Cys Asp Ala Ser Pro Ile Leu Gln Ile Thr Cys
      50           55           60
Ser Asp Thr Val Phe Ile Glu Lys Ile Val Leu Ala Phe Ala Ile Leu
      65           70           75           80
Thr Leu Ile Ile Thr Leu Val Cys Val Val Leu Ser Tyr Thr Tyr Ile
      85           90           95
Ile Lys Thr Ile Leu Lys Phe Pro Ser Ala Gln Gln Arg Lys Lys Ala
      100          105          110
Phe Ser Thr Cys Ser Ser His Met Ile Val Val Ser Ile Thr Tyr Gly
      115          120          125
Ser Cys Ile Phe Ile Tyr Ile Lys Pro Ser Ala Lys Glu Gly Val Ala
      130          135          140
Ile Asn Lys Val Val Ser Val Leu Thr Thr Ser Val Ala Pro Leu Leu
      145          150          155          160

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(2) INFORMATION FOR SEQ ID NO:21:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 481 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

(iii) HYPOTHETICAL: YES

(iv) ANTI-SENSE: NO

(vi) ORIGINAL SOURCE:

(A) ORGANISM: rat olfactory epithelium
(B) STRAIN: Sprague-Dawley rat
(F) TISSUE TYPE: olfactory epithelium

(vii) IMMEDIATE SOURCE:

(B) CLONE: J8

(ix) FEATURE:

(A) NAME/KEY: CDS

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(B) LOCATION: 2..481

(x1) SEQUENCE DESCRIPTION: SEQ ID NO:21:

C	ATC	TGC	CAC	CCG	CTC	CAC	TAC	TCT	CTT	CTC	ATG	AGT	CCT	GAC	AAC		46
Ile	Cys	His	Pro	Leu	His	Tyr	Ser	Leu	Leu	Met	Ser	Pro	Asp	Asn			
1				5						10				15			
TGT	GCT	GCT	CTG	GTA	ACA	GTC	TCC	TGG	GTG	ACA	GGG	GTG	GGC	ACG	GGC		94
Cys	Ala	Ala	Leu	Val	Thr	Val	Ser	Trp	Val	Thr	Gly	Val	Gly	Thr	Gly		
			20						25					30			
TTC	CTG	CCT	TCC	CTC	CTG	ATT	TCT	AAG	TTG	GAC	TTC	TGT	GGG	CCC	AAC		142
Phe	Leu	Pro	Ser	Leu	Leu	Ile	Ser	Lys	Leu	Asp	Phe	Cys	Gly	Pro	Asn		
			35					40					45				
CGC	ATC	AAC	CAT	TTC	TTC	TGT	GAC	CTC	CCT	CCA	TTA	ATC	CAG	CTG	TCC		190
Arg	Ile	Asn	His	Phe	Phe	Cys	Asp	Leu	Pro	Pro	Leu	Ile	Gln	Leu	Ser		
		50					55					60					
TGC	TCC	AGC	GTC	TTT	GTG	ACA	GAA	ATG	GCC	ATC	TTT	GTC	CTG	TCC	ATC		238
Cys	Ser	Ser	Val	Phe	Val	Thr	Glu	Met	Ala	Ile	Phe	Val	Leu	Ser	Ile		
	65					70					75						
GCT	GTG	CTC	TGC	ATC	TGT	TTC	CTC	CTA	ACC	CNN	NNN	TCC	TAC	ATT	TTC		286
Ala	Val	Leu	Cys	Ile	Cys	Phe	Leu	Leu	Thr	Xaa	Xaa	Ser	Tyr	Ile	Phe		
	80				85					90					95		
ATA	GTG	TCC	TCC	ATT	CTG	AGA	ATC	CCT	TCC	ACT	ACC	GGC	AGG	ATG	AAG		334
Ile	Val	Ser	Ser	Ile	Leu	Arg	Ile	Pro	Ser	Thr	Thr	Gly	Arg	Met	Lys		
				100					105					110			
ACA	TTT	TCT	ACA	TGT	GGC	TCC	CAC	CTG	GCC	GTG	GTC	ACC	ATC	TAC	TAT		382
Thr	Phe	Ser	Thr	Cys	Gly	Ser	His	Leu	Ala	Val	Val	Thr	Ile	Tyr	Tyr		
			115					120					125				
GGG	ACC	ATG	ATC	TCC	ATG	TAT	GTC	GGC	CCA	AAT	GCG	CAT	CTG	TCC	CCG		430
Gly	Thr	Met	Ile	Ser	Met	Tyr	Val	Gly	Pro	Asn	Ala	His	Leu	Ser	Pro		
			130					135					140				
GAG	CTC	AAC	AAG	GTC	ATT	TCT	GTC	TTC	TAC	ACT	GTG	ATC	ACC	CCA	CTA		478
Glu	Leu	Asn	Lys	Val	Ile	Ser	Val	Phe	Tyr	Thr	Val	Ile	Thr	Pro	Leu		
	145						150				155						
CTG																	481
Leu																	
160																	

(2) INFORMATION FOR SEQ ID NO:22:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 160 amino acids
- (B) TYPE: amino acid
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:22:

Ile Cys His Pro Leu His Tyr Ser Leu Leu Met Ser Pro Asp Asn Cys

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